A Guide to
Conditions of the Retina

FIGHTING BLINDNESS

Cure. Support. Empower.

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Conditions of the Retina

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All information current November 2014

This publication is also available online and in audio format.
Please contact us for a copy.

Foreword

On behalf of the Irish College of Ophthalmologists, I am pleased to introduce this Guide to Conditions of the Retina compiled by Fighting Blindness.

Many people in Ireland are living with severe vision loss, a significant proportion of which is due to retinal degenerative conditions. For individuals and families who have been diagnosed with a retinopathy, access to clear, relevant, detailed and easily understandable information is essential. Unfortunately, due to the rare nature of some retinal conditions, information in this format has not in the past always been readily available.

The value of providing information and support to people with conditions of the retina - as well as to the doctors who care for them - cannot be underestimated. Fighting Blindness has been doing this successfully for many years through their support services and events, and has been a real resource to Irish people who are dealing with this often life changing news. The production of this Guide to Conditions of the Retina is a shining example of a strong resource that will be invaluable to eye doctors and their patients to help them understand the conditions they are facing, as well as explaining the options that are available.

Miss Marie Hickey-Dwyer
President, Irish College of Ophthalmologists

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Our vision is to cure blindness, support those experiencing sight loss, and empower patients.

Introduction Note

Welcome to the Fighting Blindness Guide to Conditions of the Retina

More than 224,000 people in Ireland are affected by sight loss and this number is expected to rise to 275,000 by 2020. Many forms of sight loss are caused by degeneration of the layer of tissue at the back of the eye known as the retina, leading to variable levels of sight loss specific to each person and depending on the condition they have. At Fighting Blindness we believe it is vital to understand the condition that affects you or your family members, so that you can make informed decisions about your eye care and the supports that may be needed now and into the future.

The good news is that researchers are investigating the conditions and identifying the problems, with the intention of developing treatments and, ultimately, cures. Some conditions, such as certain types of age-related macular degeneration and diabetes-related sight loss, are already being successfully treated in Ireland. For other rare, genetic conditions, we are still in the early investigative stages, but positively moving from the laboratory to clinical trial stage.

The guide provides information on conditions, from basic research through to clinical trials, treatment options and relevant support services. We hope it will be a valuable and useful resource not only to individuals and families who are affected by retinal conditions, but also for the allied medical professionals who are an integral part of diagnosing, treating and caring for them.

While we have provided a substantial volume of information, we cannot expect to answer all of your questions, but we hope this resource will point you in the right direction to access further information. We also welcome you to contact us at info@fightingblindness.ie if you have any particular queries. We are here for you.

This resource has been reviewed and sanctioned by world-leading scientists and the country's leading ophthalmic specialists, and we are grateful to them for their input. We are also very grateful to Bayer Healthcare: without their support we would not be in a position to publish this important document.

Avril Daly, Chief Executive

We believe in the dignity and respect of all people affected by sight loss, and are committed to supporting people, whatever stage they are at on their own journey. We remain a patient-led organisation and ensure that the needs of people living with sight loss are always held as our highest priority.

Fighting Blindness

About Fighting Blindness

Fighting Blindness is an Irish, patient-led charity that has been funding research into treatments and cures for conditions that cause sight loss since 1983. We also provide a professional counselling service for individuals and families who are affected by sight loss, and are extremely active at national and European level in the areas of advocacy and patient empowerment. At this moment, we have almost 700 members who are affected by sight loss as well as thousands of supporters and other stakeholders who are actively involved in the organisation. We represent the 224,000 people in Ireland who are living with severe vision loss.

Founded in 1983, Fighting Blindness originally operated as a support group for people who had been diagnosed with a genetic form of sight loss. The determination of those involved moved them to act powerfully on their belief that someday treatments and cures would be available for the conditions affecting them. They knew that the key was to investigate the disorders, and that meant investing in research. We have come a long way since those early days. To date, Fighting Blindness has invested more than €15 million into research in Ireland, covering over 70 projects. We have been at the forefront of some of the most significant scientific breakthroughs in the genetics of inherited eye disease, and we are now moving into the realm of clinical trials.

We believe in the dignity and respect of all people affected by sight loss, and are committed to supporting people, whatever stage they are at on their own journey. We remain a patient-led organisation and ensure that the needs of people living with sight loss are always held as our highest priority.

Cure. Support. Empower.

The three-tiered approach of our strategy – **Cure. Support. Empower.** – informs everything that we do. We are excited and invested in the future, so we are searching for treatments and cures for sight loss. However, we know that facing a diagnosis can be extremely difficult for the individual affected, as well as their wider family and network. Often, the nature of genetic conditions means that multiple members of a family can be affected, increasing the impact of the reality of sight loss. We actively support, counsel, inform and assist people on that journey. It is also crucial that we act positively and advocate on behalf of people with sight loss to ensure that the patient voice is always heard in issues of policy, healthcare and services.

Our Purpose

Cure

Promote and facilitate the development of treatments and cures which are accessible to all patients affected by sight loss.

Support

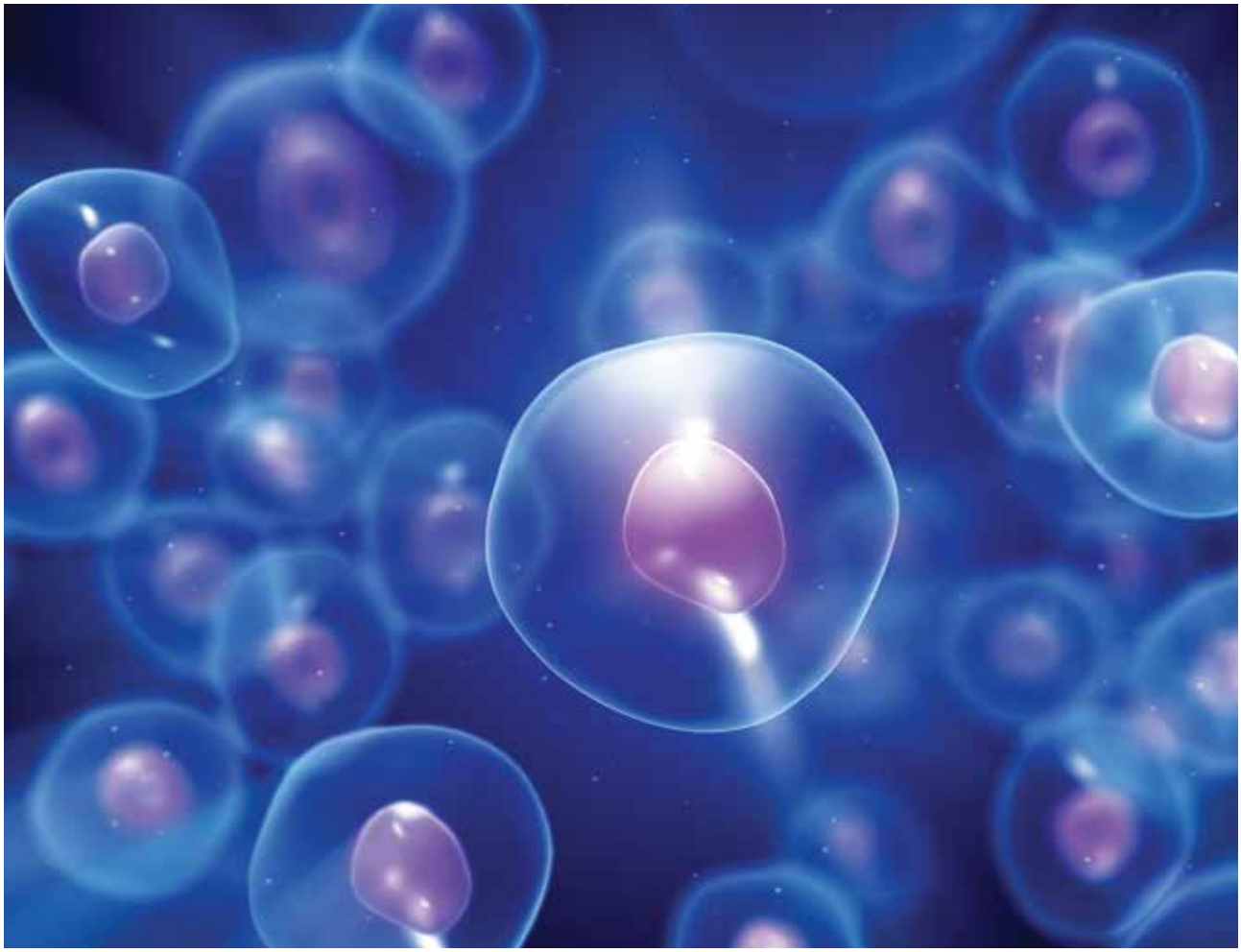
Develop our counselling service into a nationwide programme, ensuring access and support of the highest standard is available to patients and family members who are living with sight loss.

Empower

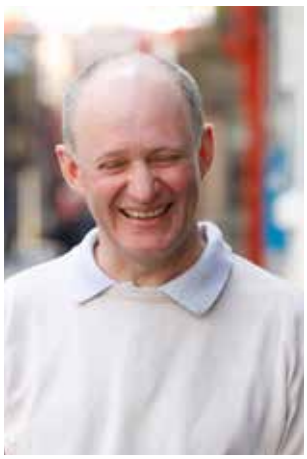
Work in partnership with all stakeholder groups in the areas of health, science, industry and government to empower patients and to achieve the greatest impact in the global fight against blindness.

My daughter rapidly lost a major portion of her eyesight when she was eleven as a result of a genetic condition called Stargardt disease. Since then Fighting Blindness have been invaluable in terms of the support, information and hope they provide through their great counselling and work towards finding cures.

Ger, Kilkenny



Insight Counselling Service



The Benefits of Psychotherapy

Sight is probably our most treasured sense, and the thought of losing it naturally gives rise to feelings of fear and uncertainty about the future. The issues that a person with sight loss faces are both practical and psychological in nature as one makes the transition from a sighted to a partially or even non-sighted lifestyle. The journey of adapting and coping with new and uninvited circumstance is unique for each individual. That needs to be understood and respected by all who offer encouragement and assistance in order to ensure that the process of adjustment is not impeded.

At such a challenging time engaging in psychotherapy can help. Working with a psychotherapist in a safe, trusting and non-judgemental environment allows the individual with sight loss the time and space to make sense of what is actually happening to them, away from the pressure of well-meaning but often ill-informed and anxious family and friends. With the appropriate support and guidance it is possible to work through and surmount difficulties to find new and life-enhancing meaning and purpose in living.

The psychotherapist offers a relationship where the person's innate inner wisdom and potential for positive change can be realised and harnessed. By freeing the natural healing process in the client, the integrity of personhood is honoured and championed. It takes time, commitment and courage to undertake such a journey but with the help and facilitation of a trained psychotherapist it is possible to reach the desired destination.

Sometimes life can be unfair. We study hard but don't achieve the hoped for grade; we train assiduously but never get picked for the first team; we work enthusiastically but are overlooked for promotion; we invest cautiously but the stock market crashes; we experience bereavement and the grief that ensues; and we risk loving another only to be rejected. But we still survive. The human being is designed to heal given the right circumstances and opportunities. We can't stop bad things happening; we can only choose how to respond. We take our life experiences and mine them for the gold of wisdom that lights our path through dark and alien territory. We grow and evolve so that sight loss informs but does not have to determine how we live our lives.

It is not just the individual with sight loss who is affected but also their partner, children, extended family and friends. At Insight, we work with all those affected directly and indirectly by sight loss. We offer a range of services including psychotherapy, support groups and technological assistance in conjunction with other relevant agencies.

Sight loss is a life changing experience, but not a life ending one. We are here to help.

John Delany, Senior Counselling Manager
Insight Counselling Service

Insight Counselling Service

The Insight Counselling Service is a professional counselling service for people and families who are affected by sight loss.

The centre was established by Fighting Blindness in 2002 to help people cope with the challenges of being diagnosed with, and living with, conditions that cause sight loss. Losing your vision can also impact your family and friends, so the service can help those close to you adjust to new challenges as well.

No matter what your level of sight loss, we are here to help and provide any support you may need. We offer a variety of services and invite you to get in touch if there is anything that you feel may be of benefit to you.

The Insight Counselling Service can be contacted using the details below:

Email: insight@fightingblindness.ie
Please contact Fighting Blindness on 01 6789 004 and we can put you in contact with the Insight Counselling Service.

Support Services

Crisis Counselling
Crisis counselling can help individuals deal with an upsetting event or situation by offering assistance and support while aiming to improve a person's coping strategies in the here and now. It is usually for a short period of time.

Long Term Psychotherapy
This involves developing a therapeutic relationship over time with a therapist in order to address mental health concerns or to deal with a source of life stress. It can help the person to develop skills for dealing with or overcoming stress, worries, problematic thoughts or behaviours.

Couples' Therapy
This type of support is often very useful in providing a safe and private setting for a couple to work through challenges together whether in their relationship or as a result of external circumstances. It is important that each partner in the relationship feels like they have equal say, in a balanced session.

Family Support
Family sessions can involve everyone and can be comprised entirely of adults, or can involve children too, if suitable. It provides a setting that is respectful of each person's position so that when the family group is leaving, they all feel that they've had a chance to be heard and understood.

Support Groups
In support groups, the individuals support each other, while the therapist facilitates and ensures that nobody is dominating the session. These sessions are about sharing experiences as opposed to telling another person what to do. They provide a safe environment which encourages people to interact. These groups are organic and develop around the needs on that particular day, rather than following a set programme. We currently hold monthly support groups in Dublin, Cork and Limerick on the first Wednesday, last Wednesday and third Thursday of the month respectively.

Telephone Support
For people living outside of Dublin or for those who are unable to travel, we offer a telephone support service. This service can also be helpful for someone who needs an immediate response.

Information about Conditions

We endeavour to provide information to people who have been diagnosed with a retinal condition as well as providing updates on any research that may be developing in that area. We do this in several ways through reports and updates on our website and in our published materials, as well as through the public engagement day at our annual Retina Conference. We are also very happy to discuss this over the phone through the Fighting Blindness office.

Connect with Other Services

We can help you to identify any other services which may be of benefit to you. These services include organisations such as the NCBI-the national sight loss agency, the Irish Guide Dogs, and ChildVision who offer training in mobility, independent living skills, visual aids and assistive technology amongst other services.

Hospital Supports

We provide support services at the Research Department of the Royal Victoria Eye and Ear Hospital in Dublin every Wednesday and Thursday morning, and the Mater Hospital Eye Clinic in Dublin each Thursday morning.

The Exchange Club

This era of fast moving technology offers people who are visually impaired an opportunity to improve the quality of their communications with others, using such equipment as mobile phones with Talks, iPhones with voiceover and interface with laptops, etc. The Exchange Club is a place for people with a visual impairment to meet friends and help each other to get the best use of such technology. The Exchange Club meets on Monday mornings from 11am to 1pm. For further information, please contact Fighting Blindness on 01 6789 004 or email insight@fightingblindness.ie.

How will I provide? I was married with two children and another one on the way when I was diagnosed with Ushers in 1999. Fighting Blindness provided me with invaluable support in counselling and group meetings. I met some incredible people. It's important to talk.

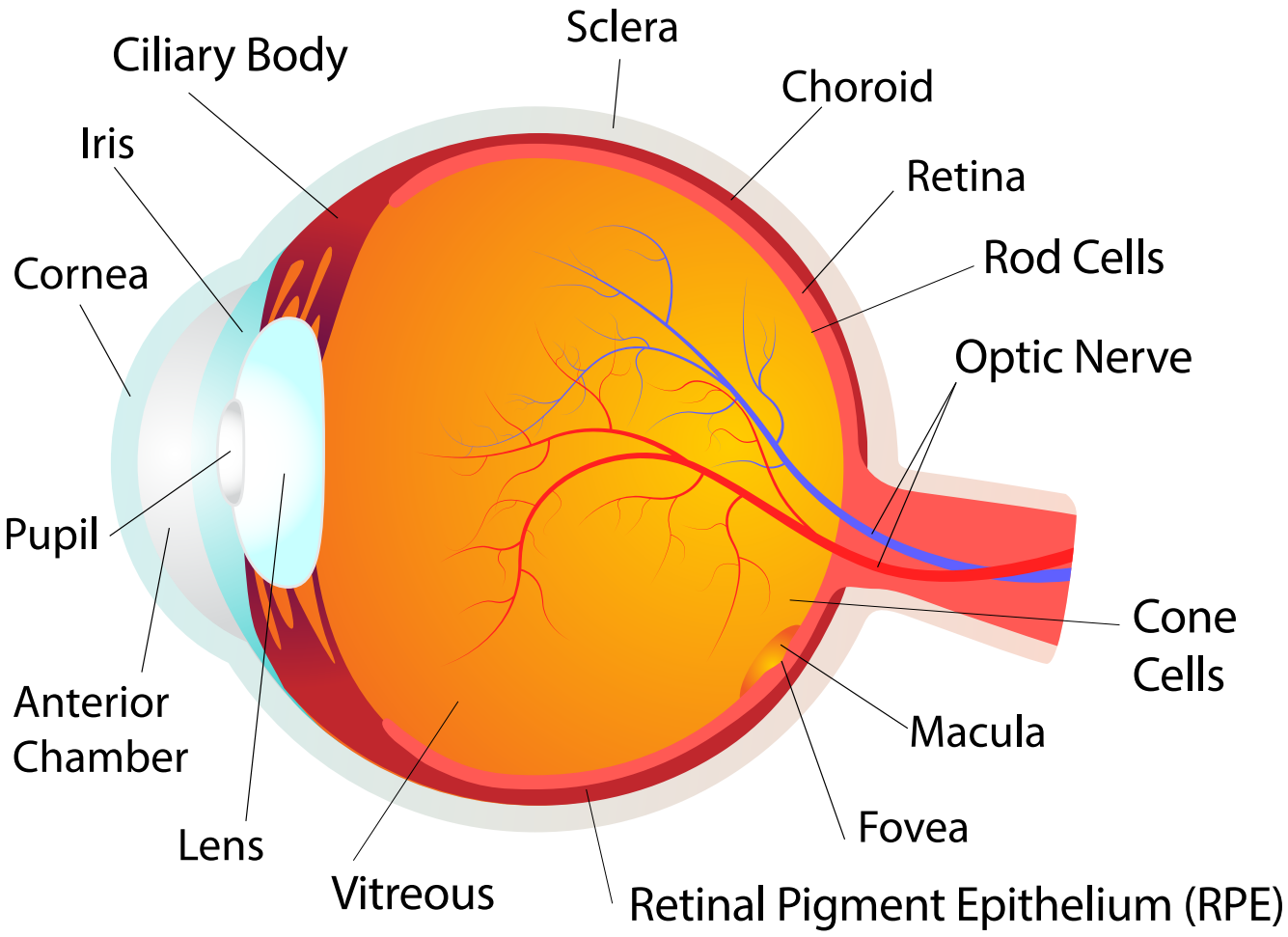
Dave, Dublin

The eye is one of the most complex organs in the body. There are many parts that make up the eye, all of which are necessary for the eye to function properly.

Your Eyes

How Your Eyes Work

Light rays enter the eye through the cornea, pupil and lens. These light rays are focused onto the retina, the tissue lining the back of the eye. The retina converts light rays into impulses which are then sent through the optic nerve to the brain, where they are recognised as images.



Parts of the Eye

Cornea: The cornea is the transparent outer layer of the eye that refracts, or redirects, light to a sharp focus at the retina.

Lens: The lens is a transparent structure inside the eye that works with the cornea to focus. It fine-tunes images and allows us to see at various distances.

Iris: The iris is the visible outer layer that gives us our eye colour. It adjusts the size of the pupil, determining how much light reaches the retina.

Pupil: The pupil is the hole in the centre of the eye that lets light in. It gets smaller in bright conditions to let less light in and bigger in dark conditions to let more light in.

Retina: The retina is a light-sensitive tissue that lines the back of the eye. It consists of rod and cone cells. These cells collect the light signals directed onto them and send them as electrical signals to the optic nerve at the back of our eye.

Macula: The macula is the central part of the retina that allows us to achieve high-quality vision and accounts for our ability to read, to drive safely and to see the world in detail and colour. The macula is yellow due to the collection of pigment from coloured fruit and vegetables we eat as part of our daily diet.

Fovea: The fovea is the centre of the macula which provides the sharp vision.

Rod Cells: Rod cells are concentrated around the edge of the retina. They help us to see things that aren't directly in front of us, giving us a rough idea of what is around us. They help us with our mobility and getting around, by stopping us from bumping into things. They also enable us to see things in dim light and to see movement.

Cone Cells: Cone cells are concentrated in the centre of our retina where the light is focused by the cornea and lens. This area is called the macula. Cone cells give us our detailed vision which we use when reading and looking at people's faces. They are also responsible for most of our colour vision.

Retinal Pigment Epithelium (RPE): The retinal pigment epithelium is a layer of cells located just outside the retina and is attached to the choroid.

Choroid: The choroid is a layer containing blood vessels that lines the back of the eye; it is located between the retina and the sclera.

Sclera: The sclera is the white outer coat of the eye, surrounding the iris.

Optic Nerve: The optic nerve carries information of what you see from the retina to the brain.

Vitreous: The clear, jelly-like substance found in the middle of the eye that helps to regulate eye pressure and shape.

The Spectrum of Sight Loss

Most people who have a visual impairment are able to see something. The level of vision can vary from being able to distinguish between light and dark, to seeing large objects and shapes, to seeing everything but as a blur. Visual impairment is a term used to describe all levels of sight loss. It covers moderate sight loss, severe sight loss and blindness. People are not either sighted or blind; there are different degrees of sight loss and different ways in which sight loss can affect a person's vision. For example, some conditions can affect the peripheral vision, and others can affect the central vision. Sight loss can affect people of all ages and can have an impact on all aspects of a person's life: social, school and work, and everyday tasks.

What You Can Do to Take Care of Your Eyes

No matter what your level of vision, it is important to look after your eye health and protect whatever sight you do have. There are a number of factors that can exacerbate or contribute to certain conditions, so it is important to be aware of them. The list below explains what you can do to take care of your eyes.

1. Have Regular Eye Tests

It is recommended that people have an eye test every two years. A regular eye test can identify any early indications of diseases, some of which are treatable if caught early. It is important to maximise any useful vision you have by wearing the best possible prescription, your optometrist can help you with this.

2. Don't Smoke

Your eye is a complex organ that needs oxygen to survive; smoking reduces the amount of oxygen in your bloodstream, so less oxygen reaches the eye. This causes oxidative stress and damages the retina and also causes cell death to retinal pigment epithelium (RPE) cells. Smoking is a risk factor for developing age-related macular degeneration and diabetic retinopathy. Stopping smoking can stop or reverse damage to the eyes, depending on the severity of the condition. Passive or second-hand smoke also causes damage to the eye and should be avoided. You can find information about how to quit smoking at www.quit.ie.

3. Wear Sunglasses

Ultraviolet (UV) light from the sun's rays can cause damage to your eyes. To reduce risks always wear sunglasses when in the sun. Check your shades have a UV factor rating and block 100 percent of UV rays. Your sunglasses should carry the CE mark, which indicates that they meet European safety standards. Close-fitting wraparound glasses will block more light and offer better protection. Be aware that UV rays can still cause damage when it is cloudy and overcast.

4. Eat the Right Food

Some foods can help protect against certain eye conditions, like cataracts and age-related macular degeneration due to the specific nutrients they contain. These nutrients are called lutein or zeaxanthin, and are found in many fruits and vegetables including mango, squash, broccoli, green beans, and spinach.

5. Take Regular Screen Breaks

If you use a computer, take frequent breaks from your screen – at least once an hour. Resting your eyes can help you avoid headaches, eyestrain and soreness.

Healthcare Professionals Who Look After Your Eyes

There are a number of different healthcare professionals that you may interact with when it comes to looking after your eyes, including opticians, optometrists, ophthalmologists and orthoptists. Each of these professionals has a different role in caring for eye health, explained below.

What is an optician?

Opticians are technicians trained to design, verify and fit lenses and frames, contact lenses, and other devices to correct eyesight.

What is an optometrist?

Optometrists are healthcare professionals who provide primary vision care ranging from sight testing and correction to the diagnosis, treatment, and management of vision changes. An optometrist is not a medical doctor.

What is an ophthalmologist?

An ophthalmologist, also called an eye doctor, is a medically trained doctor who has undertaken further specialist training and study in the human eye. In the Republic of Ireland there are two types of Eye Specialists; Medical Eye doctors who undergo 11 years of clinical medical training, and Eye Surgeons who undergo on average 14 years of clinical medical training.

What is an orthoptist?

An orthoptist is an allied health professional involved in the assessment, diagnosis, and management of disorders of the eyes, extra-ocular muscles and vision. Orthoptists are an important part of the eye care team and work in close association with ophthalmologists, usually in a hospital based setting. They are involved in many areas of care, including paediatrics, neurology, community services, rehabilitation, geriatrics, neonatology and ophthalmic technology.

What Happens at Your Ophthalmology Appointment?

When you visit your ophthalmologist, you will be asked to perform a number of tests that measure different parts of your vision and look at different parts of your eyes. Some of the tests are very quick and straightforward while others will take more time as they require drops in your eyes to take affect before they can be performed. Some of the tests require you to look at something and respond about what you see. Your ability to perform these tests will depend on your level of vision, and some people may find them difficult or frustrating. Other tests involve the measurement of involuntary responses of the eye or taking photographs of the eye. Some of the tests that are used are explained below. If you have any questions about any of the tests or are unsure of anything taking place during your appointment, don't be afraid to ask your ophthalmologist or test technician to explain it you.

Visual Acuity Testing
Most people are familiar with visual acuity testing, which involves reading letters from a chart while sitting or standing a certain distance away. The purpose of this test is to measure your central vision which is the ability to see fine detail.

Colour Testing
This test measures your colour perception. You will be asked to look at a series of images composed of many small circles. Someone with normal colour vision can recognize numbers within the images.

Visual Field Testing
This test measures the scope or range of vision, including peripheral (side) vision and central vision. A light is brought in from the side on a screen, and slowly moved to the centre of vision. You are asked to press a button as soon as you see the light.

Electroretinogram (ERG)
This measures the electrical response of the light-sensitive cells in the eye, the rods and cones. It also measures retinal function. Prior to this test, you will be given drops in your eyes to dilate the pupils. You will also be given an anaesthetic eye drop to numb your eyes. A special type of recording contact lens will then be placed over your eye and electrodes will be placed on the skin near the eye. You will be asked to watch some flashing lights; these are used to stimulate the retina. The electrodes measure the electrical response of the retina to the flashing lights. The test will be performed first in a dark room and then again when the lights are turned on. The test does not cause any pain, but some people may find it uncomfortable. Because of the drops used, you may notice that your vision is blurred for quite some time afterwards.

Fundus Photographs
This test takes a photograph of the retina fundus at the back of the eye using a special camera. The images will show any changes or abnormalities in the back of the eye. You will be given drops to dilate your eyes before this test.

Fluorescein Angiogram
During this test a special dye, called fluorescein, is injected into the bloodstream. The dye is injected through the arm. Its purpose is to highlight the blood vessels in the back of the eye so they can be photographed. This makes it easier for a doctor to see abnormalities in the back of the eye.

If you have any questions about anything that happens at your appointment or are unsure about any of the information you receive, don’t be afraid to ask your ophthalmologist or test technician to explain it you.

Questions to Ask your Doctor

You may feel overwhelmed by the information you receive at your appointment so it can be useful to make a list of questions beforehand to take with you. Here are some suggestions that might be helpful;

- **What is my diagnosis?**
- **How will my vision be affected?**

  A doctor will not be able to give you an exact answer to this question as everyone is different, and conditions can progress at different rates in different people. They will be able to tell you which parts of your vision are most likely to be affected, for example, your central vision or peripheral vision.

- **How will it affect my home and work life?**

  The doctor may be able to give you an example of how the condition will affect an everyday task such as reading or driving.

- **What is the short-term and long-term prognosis for my disease or condition?**

  Many conditions will cause your vision to change over time. A doctor will not be able to give you an exact prognosis or time line but may able to give you an idea of what can happen in the short and long term in most cases of your condition.

- **What caused the disease or condition?**

  Is your condition genetic or can it be affected by lifestyle or environmental factors.

- **Are there local agencies or organisations that can help me learn more about my condition and vision loss?**

  There may be an organisation or support group that deals specifically with your condition, or that may be able to give you more information.

- **Has my vision changed since my last visit?**
- **Could medication or health supplements I take have any effect on my vision?**

  If this is something you are unsure about, bring a list of any medications or supplements to your appointment and ask your doctor about them.

The importance of Fighting Blindness in the development of the genetics lab in TCD and the progress of our research into retinal conditions cannot be over-emphasised. Without the initial funding provided by the group in the 80's, we would not be at the stage we are at now where we are moving towards potentially the first gene therapy for the most common cause of RP.

Prof Jane Farrar, Trinity College Dublin

Research

Fighting Blindness Research

Since it was founded in 1983, Fighting Blindness has invested over €15 million in more than 70 research projects. In 1989, researchers in Trinity College Dublin, funded by Fighting Blindness, were the first in the world to identify the Rhodopsin gene, the first gene implicated in the condition retinitis pigmentosa (RP). Since then we have relentlessly pursued solutions to different causes of sight loss. Our work focuses on rare inherited and age-related retinal degenerative diseases.

Fighting Blindness investigates every realistic avenue of medical research that has a clear potential to result in therapeutic interventions for people living with all forms of sight loss. Over the past number of years, we have broadened our scope from funding genetic research to looking at new and emerging technologies, particularly cell-based technologies and population studies. Basic and translational research remains key to our research strategy through our five pillars of research.

Our Five Pillars of Research

Genes and Gene Therapy
The theory behind gene therapy is to treat the disease by repairing the abnormal gene. This is achieved by replacing the disease-causing faulty gene with a “normal” copy into an individual’s cells. The most successful method to deliver the gene to the cells is by using a harmless virus that has been genetically modified to carry human DNA. The eye has proved to be an ideal organ for gene therapy as it is well protected from the body’s immune response. These early successes are paving the way in the near future for treatments for both inherited and non-inherited forms of blindness.

Cell Therapy and Regenerative Medicine
Stem cell technology holds great potential for improving the sight of people with a visual impairment, particularly to replace photoreceptors that have been lost due to degeneration. A number of studies are currently being undertaken in order to develop new therapies to treat, or prevent a loss of vision. Central to this research is the development of our understanding of how different types of stem cells behave, and how best to harness their potential in the eye. It is important to realise that stem cells are not a one-stop, generic cure, but they do hold exciting potential for vision repair.

Retina Implant Technology
Retina implant technology involves the use of microelectronics and microchip electrodes surgically implanted into the back of the eye (retina) to restore the function of the damaged light-activated cells found there. These photoreceptor cells respond to light and convert it to an electrical signal which is passed to nerve cells in the eye, and then ultimately to the brain where it is perceived as vision.

Novel Drug Therapy
Sustained scientific research has led to a better understanding of the underlying cause of disease for a large number of retinal degenerative conditions. These efforts have led to the exploration of novel drug therapies to “compensate” for the defective part of how vision is processed. Another approach involves using drugs to target pathways that may slow the death of photoreceptor cells, thus preserving vision for longer. Many of these drugs are repurposed drugs; they may already be approved for use in a completely different disease and are being tested for their effectiveness in the eye. These therapies are attractive as they may have the potential to be administered to many different genetic subtypes independent of the causative gene for the degeneration.

Population Studies
Population studies, also known as epidemiology, is the study of a group of individuals taken from the general population who share a common characteristic, such as a health condition. Our Target 5000 research project is a good example of this type of study. You can read more about Target 5000 on page 41 of this booklet.

Clinical Trials

What is a Clinical Trial?

Clinical trials are medical research studies in which people volunteer to participate. Carefully conducted clinical trials are the safest and fastest way to find treatments that work in people. A clinical trial is used to evaluate the safety and effectiveness of a new procedure, medication or device to prevent, diagnose or treat an eye disease or disorder.

There are four different phases to a clinical trial. The time from a phase one to a phase four trial can take many years.

Phase 1 Trial
These are the earliest trials in the life of a new drug or treatment. They are usually small trials, recruiting anything up to about 30 patients. Phase 1 trials are undertaken to determine the safety of a potential treatment. People recruited to Phase 1 trials often have advanced eye disease.

Phase 2 Trial
A phase two trial tests the potential new treatment in a larger number of volunteers, to learn more about how the body responds to the treatment, the optimal dose of the treatment and how the treatment affects a certain eye condition. If the results of a phase two trial show that a new treatment may be as good as an existing treatment or better, they move to phase three.

Phase 3 Trial
Phase three trials are usually much larger than phase one or two, sometimes involving hundreds or thousands of patients in many different settings. Phase three trials are usually randomised. This means the researchers put the people taking part into two or more groups at random. One group gets the new treatment and the other the standard treatment or a placebo (non-active) treatment.

Phase 4 Trial
Phase four trials are performed after a drug has been shown to work and has been granted a license. They are performed in order to understand more about the treatment, by evaluating its safety and effectiveness in larger numbers of patients, subgroups of patients, and to compare and/or combine it with other available treatments.

Fighting Blindness is committed to aiding the discovery of new treatments for eye diseases through research and ensuring they are implemented in Ireland through advocacy. This unified vision of Fighting Blindness Ireland is integral to all we wish to achieve.

David Keegan,
Consultant Ophthalmic Surgeon
Mater Hospital Dublin

Human Genetics – A Brief Insight

Each human individual is composed of approximately ten to one hundred trillion cells. Each one of these cells has a control centre called a nucleus where vital information is stored. The nucleus enables the correct components of the cell to be formed so that the cell can function efficiently. Our genetic material, called deoxyribonucleic acid (DNA), is found in the nucleus of the cell. In humans, the DNA is divided among the chromosomes in the nucleus. Almost all cells in a human have 23 pairs of chromosomes. It is just the cells involved in reproduction, that is, ova and sperm that have a single set of chromosomes – egg and sperm cells simply have 23 chromosomes. In this way when an egg is fertilised, the correct number of 23 pairs of chromosomes is reconstituted.

The chromosome material is made of DNA, and this DNA is wound around proteins called histone proteins. The DNA found in human chromosomes contains the genetic code that enables cells to function properly. The human genetic code has three billion letters (akin to a book with a million pages). These letters are called nucleotides or bases; the whole code is termed the human genome. Approximately one in 1,000 letters of code varies between each human, which means that we are 99.9% the same as each other. Although the human genome comprises three billion letters of code found in 23 pairs of chromosome in each cell, this vital material is highly compacted and tightly packaged into the nucleus. Indeed there are about two meters of DNA extremely tightly packaged into every nucleus of every cell. As each person has ten to one hundred trillion cells, they have hundreds of thousands of kilometres of DNA in their body.

What does the genetic code / your genome do?

The genome codes for the key components that enable each of your ten to one hundred trillion cells to survive and to function properly. Major building blocks in your cells are the various proteins the cells contain. The genetic code has sections within it (involving approximately 2% of the total genetic code) that are dedicated to supplying the information that will allow the correct proteins with the correct sequence to be generated in cells. Each section of DNA that encodes a protein is given the term “gene”. Humans have approximately 20,000-25,000 genes, found in the DNA of the 23 pairs of chromosomes in the nucleus. The letters of code in the DNA are translated into a language of proteins, so that the sequence that the protein has is directly related to the sequence that the section of DNA or gene has.

So what about genetic disorders?

Given that the DNA code is directly related to protein sequences, it is therefore not surprising that when the DNA code has a mistake or a mutation in it, if this occurs in a region of the genetic code that is dedicated to making a protein, then an incorrect protein with a mistake in it will be generated. If this protein in turn has a vital function in the cell, the cell may not function properly and indeed may possibly die. This is the basis of many genetic disorders. There are over 3,000 genetic diseases in humans that are caused by a mutation in one of the 20,000 - 25,000 genes found in the human genome. These disorders, involving a mistake in just a single gene, are called Mendelian disorders.

So what is the relevance of this to patients and human health?

We are now in the era of "genomics" and what is termed the era of "big data" where it is possible to obtain the DNA sequence of someone's genome quite rapidly and generate large amounts of data. The genomics revolution enables scientists to begin to understand which genes are causative of which disorders. In essence, this means that one can begin to decipher for a given patient what may be the underlying genetic cause of their disorder. Next generation sequencing (NGS) technologies can be used to rapidly sequence parts of a patient's genome, which is what Fighting Blindness is doing as part of the Target 5000 project which you can read about on page 41 of this booklet. Importantly it also enables scientists and clinicians to develop therapies that are directed towards the primary cause of a disorder – this is termed rational drug design where, for example, genetic information is used to develop innovative therapies that are targeted to correcting the precise problem and hence notably may represent more effective treatments. For example for a patient who does not have a normal copy of a gene (a copy without a mutation), delivering a normal gene represents a logical solution for many genetic disorders. There are to date approximately 1,900 gene therapy trials in humans reported; encouragingly some of these therapies in trial have provided real benefit to patients (www.clinicaltrials.gov).

Mitochondrial disorders and the mitochondrial genome

While the DNA found in 23 pairs of chromosomes in the nucleus of human cells represents the majority of DNA present in every cell of an individual's body, there is one notable exception. Surrounding the nucleus is what is termed the cell cytoplasm. The cell cytoplasm is enclosed from other cells by the cell membrane. Much of the machinery of the cell is found in the cell cytoplasm. A really vital part of this cellular machinery is found in structures termed 'mitochondria'. These are structures (or organelles) that are central to generating the energy that enables a cell to function. This energy is in the form of ATP and is essential for the many functions that any cell undertakes – the mitochondria are called the 'power houses' of the cell. The mitochondria in the cell cytoplasm have their own DNA or genome. The mitochondrial DNA genome is much smaller than the DNA genome in the nucleus, just approximately 16,600 letters of code versus three billion. In each cell there are hundreds of mitochondria, and in each mitochondria there are between two to ten copies of the mitochondrial DNA genome. It turns out that mistakes or mutations in the code of the mitochondrial genome can also give rise to disorders – these are called mitochondrial disorders. One such mitochondrial disorder is Leber hereditary optic neuropathy (LHON) which causes significant visual loss and for which a number of gene therapies are under development. See page 60 for more information on mitochondrial disorders.

Future perspective

There are so many questions that are still to be answered, however, the technologies that allow scientists to address such questions are improving rapidly. Undoubtedly there are exciting times ahead with significant scientific discoveries and the development of effective therapies within our grasp; such advances should improve the quality of life for patients with both genetic and acquired disorders.

Prof Jane Farrar, TCD

Inheritance Patterns

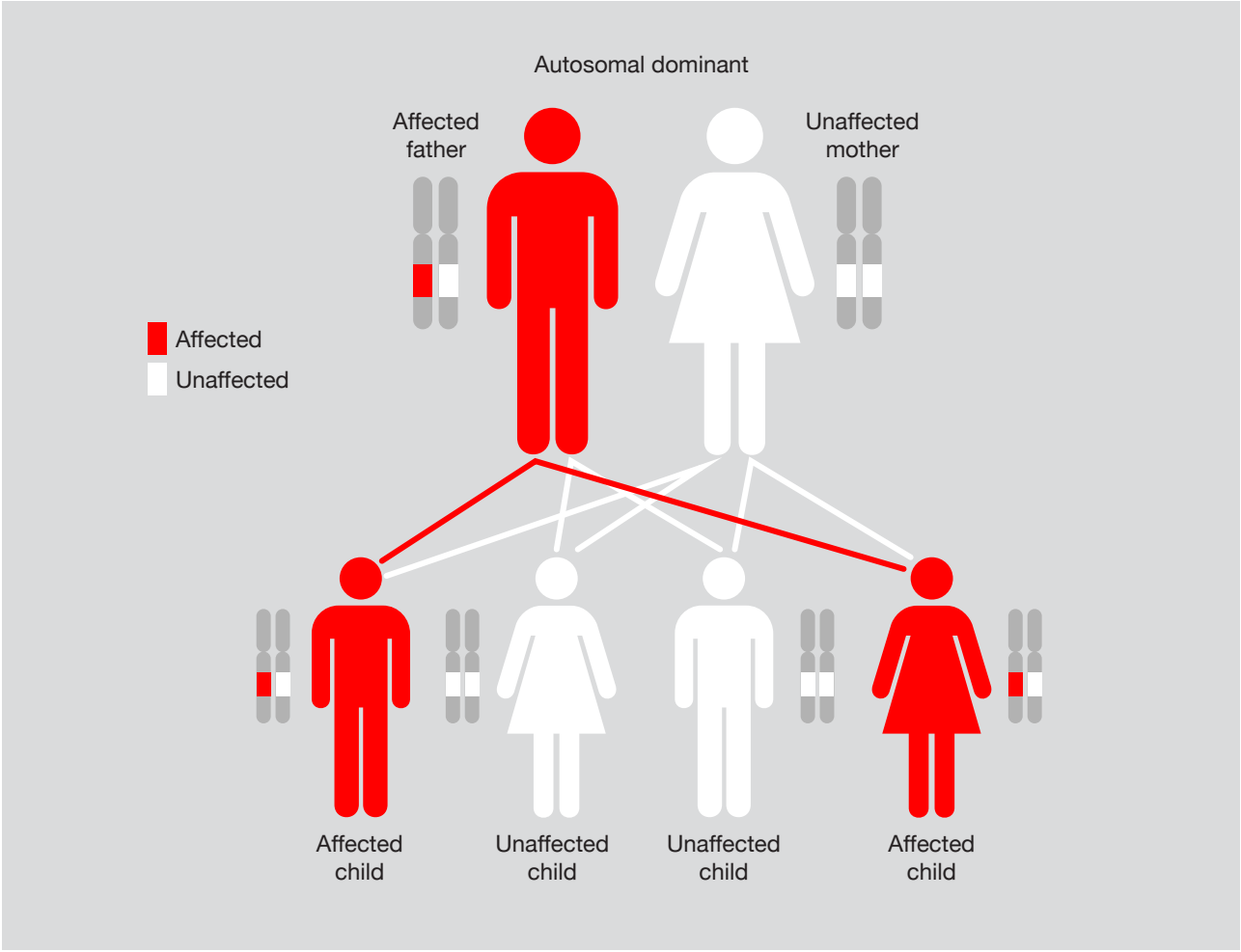
What are the different ways a genetic disease may be inherited?

The diagrams of family trees, also known as pedigrees, are shown below and these illustrate the different ways in which inherited retinal degenerations can run in families. An affected person is shown in **red** and an unaffected person is shown in **white**.

Autosomal Dominant Inheritance

Autosomal dominant inheritance occurs when just one copy of a gene mutation is enough to cause an individual to become affected by the condition. The mutation can lead to development of the condition even when the second copy of the gene is normal. Each affected person usually has one affected parent, and these disorders tend to occur in every generation of an affected family.

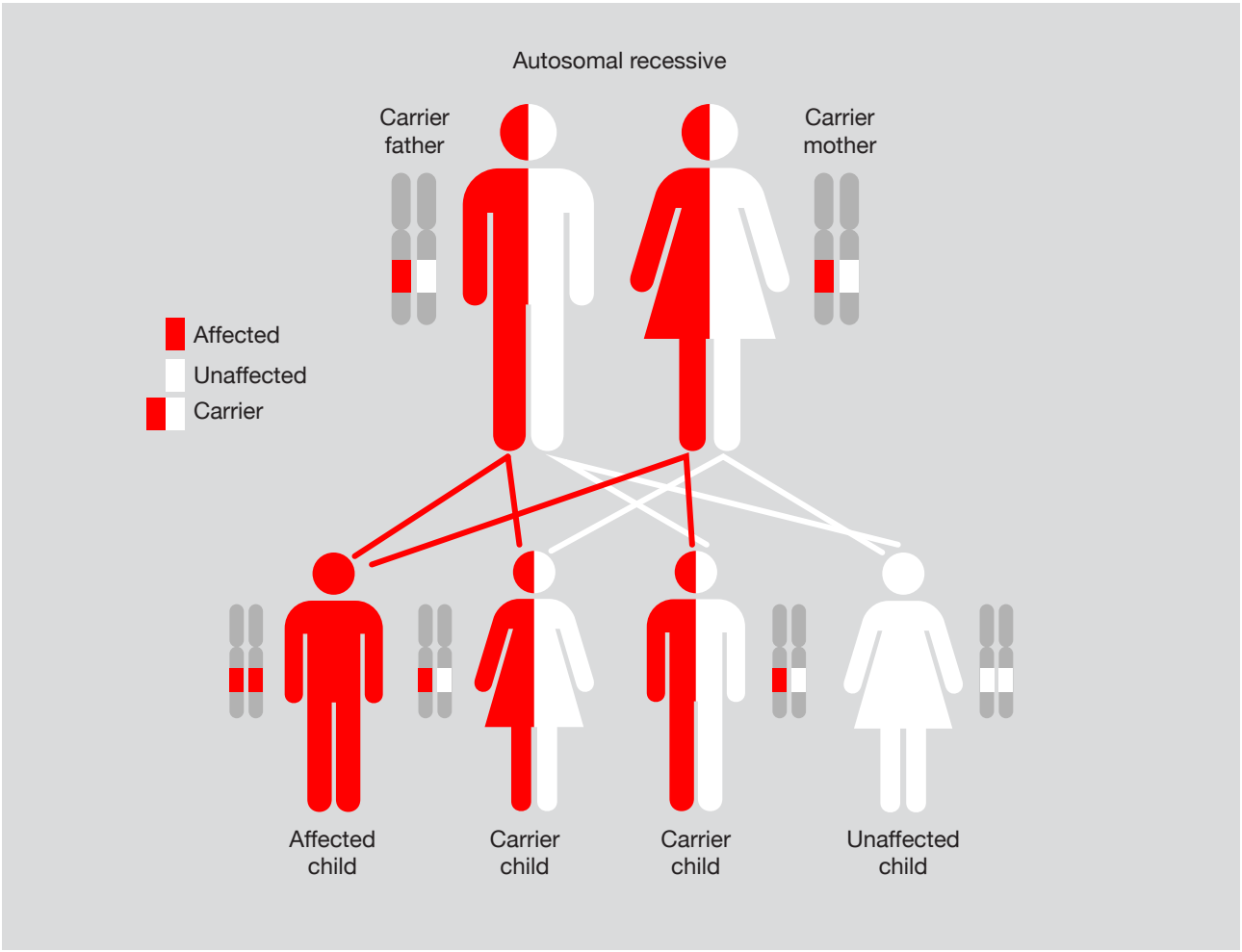
Both males and females can be affected, however some may be affected so mildly that they may not even be aware that they have signs of the disease. In rare cases, someone with a dominant mutation may not show any signs of the condition. In autosomal dominant inheritance, each affected individual has a 50%chance with each pregnancy of having a child affected by the condition.



Autosomal Recessive Inheritance

In autosomal recessive inheritance, on the other hand, a person develops the condition only when both copies of the gene don't work. That is, the gene from the mother and the gene from the father both have mutations and the affected person inherited one gene mutation from each parent.

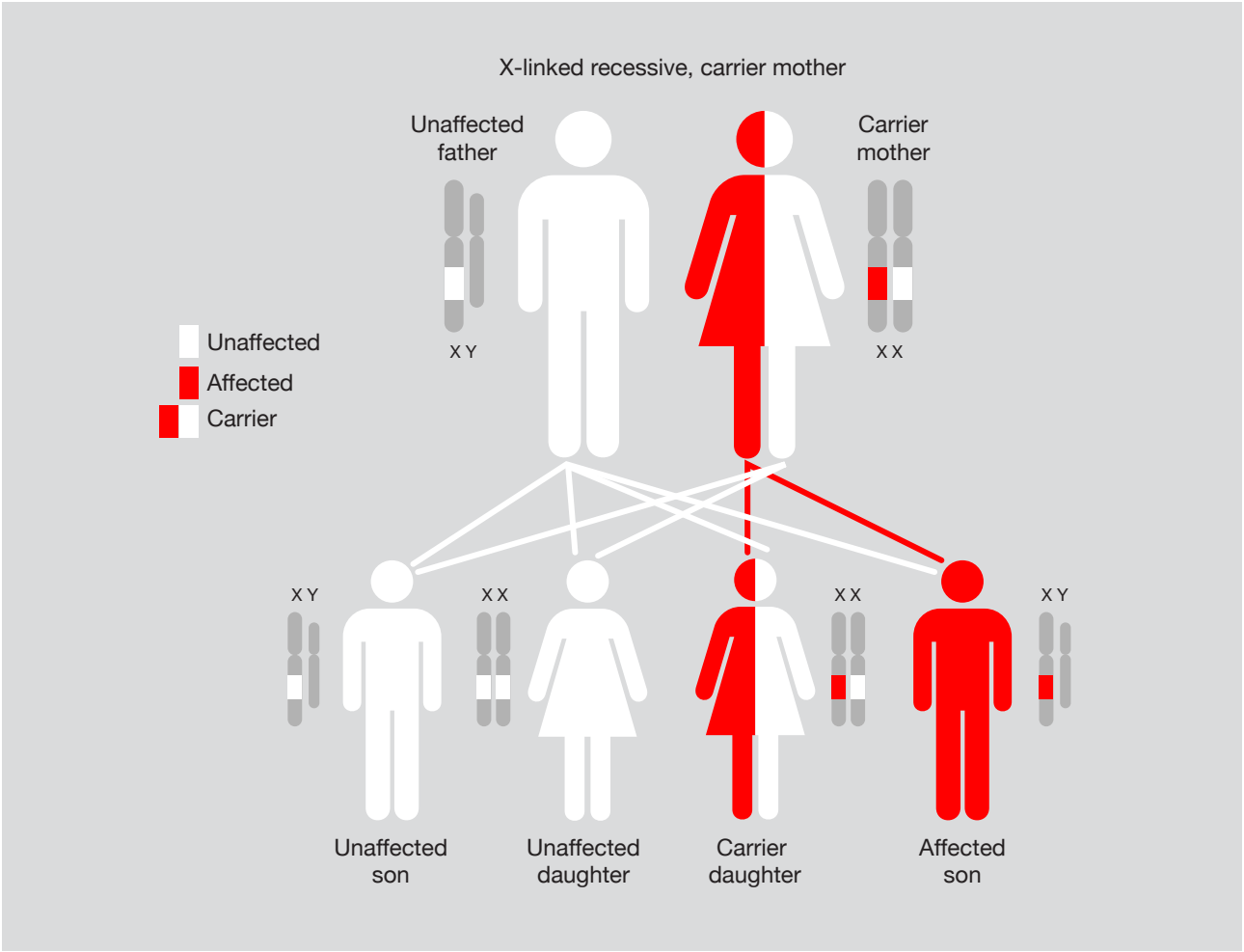
Typically, only one generation is affected and both males and females can be affected. In this type of inheritance people with one mutated copy of the gene do not have the condition, but they are called 'carriers'. When both parents are carriers, there is a 25% chance with each pregnancy that they child will have the condition.



X-linked Recessive Inheritance

In X-linked recessive inheritance, the mutation is on the X chromosome. Males have an X and a Y chromosome and females have two X chromosomes. Because males have only one X chromosome, if they inherit a disease mutation on that chromosome, they will develop the condition. Females with one mutation and one regular copy of the gene typically do not show signs of disease, although due to the phenomenon of non-random X chromosome-inactivation, some female carriers may display symptoms.

In families, multiple generations of affected males are observed, connected through unaffected females. For example, an affected grandfather might have a daughter who is a carrier and she may then have a son who is affected. When a male is affected, all of his daughters will be carriers and none of his sons will be affected. When a female is a carrier, each daughter has a 50% chance of being a carrier and each son has a 50% chance of being affected.



Mitochondrial Inheritance

Mitochondrial inheritance, also known as maternal inheritance, applies to genes contained within mitochondrial DNA. Mitochondria are structures within each cell that convert molecules into energy. Because only egg cells and not sperm cells contribute mitochondria to a developing embryo, only females pass on mitochondrial mutations to their children. These conditions can affect both males and females and can appear in every generation of a family, but fathers do not pass down these conditions to their children. The severity of symptoms may vary from one affected individual to another; even within the same family due to a 'dosage' effect. This is due to the fact that we have many mitochondria in each cell. In one individual, if only a small proportion of mitochondria in each cell have the mutation, symptoms will be mild. In another individual, if a higher proportion of mitochondria in each cell carry the mutation, symptoms will be more severe.

Uncertain Inheritance

Very often, a person diagnosed with an inherited condition has no other family members with the disease. There are several possible reasons for only finding one person affected in the family. The mutation may be a new event in that person, or other family members may have the same mutation, but may have not yet been diagnosed with the condition. They may have a later age of onset, or have milder signs of the disease. The mutation might have been in the family for a long time, but by chance, no other family members have been affected. For autosomal recessive disease, carriers may have been present in the mother's and father's side of the family for several generations, but a child won't develop a condition unless both parents are carriers and both pass on a mutation to their child.

The Research Foundation at the Eye and Ear Hospital, Dublin has been working with Fighting Blindness and the Genetics Department at Trinity College Dublin from the very beginning to spearhead world-class research into inherited retinal degenerations. This work, initiated by Fighting Blindness, has made a major contribution to the worldwide effort to identify the genetic basis for many of these conditions and pave the way for future treatments. While past achievements have been significant, I firmly believe that, working together, the best is yet to come.

Dr Paul Kenna, Trinity College Dublin and Royal Victoria Eye and Ear Hospital

Target 5000 – Gateway to Vision

Our Target 5000 research project aims to provide genetic testing for the estimated 5,000 people in Ireland who have a genetic retinal condition. These conditions include, among others;

- Retinitis Pigmentosa (RP)
- Usher Syndrome
- Stargardt Disease
- Leber Hereditary Optic Neuropathy (LHON)
- Leber Congenital Amaurosis (LCA)
- Choroideremia
- Retinoschisis

Why is genetic testing important for me?

Until now, one of the challenges confronted by someone who has one of these conditions was the lack of a precise diagnosis. It's often impossible to tell which specific type of retinal disease a patient has based on just looking at the eye, because inherited retinal diseases are some of the most complicated of all genetic conditions, involving more than 200 genes. Receiving a complete diagnosis requires genetic testing. Through genetic screening of the person affected and their family members, Target 5000 will provide more detailed information about the nature and inheritance pattern of the condition.

How does it work?

The researchers will use DNA sequencing to try to find the gene that is mutated and causing the condition. This can be looked at like peeling an onion: First they look at the outside layer which contains the known genes associated with retinal degenerations. There are approximately 200 genes known so far, and these are estimated to account for conditions in about 60% of people affected. If your gene is in this first outside layer then finding the gene is relatively straightforward. However if the gene is not found in this outside layer then further work is needed to look at your entire genome. This will take a longer time, but the technology is constantly being refined and so this may happen sooner than we expect.

What happens when they find the gene mutation causing my condition?

When a causative mutation is discovered, you will be contacted by the hospital and an appointment will be set up so that you can receive the results of your genetic tests. Information about your gene and condition will then be added to a national patient registry. This registry will enable us to identify patients who are eligible for clinical trials. Research projects have now advanced through basic research to first stage clinical trials. Many of these therapies will rely on repairing the specific gene abnormality for each individual. That is why it is vital that we identify the exact genetic profile of people affected by a retinal degenerative condition in Ireland.

How can I get involved?

You can register for Target 5000 by contacting our research manager on 01 6789 004 or target5000@fightingblindness.ie. You will be asked to provide some basic information including personal details and details about your condition. This information is confidential and stored in a secure file accessed only by the research manager.

What happens next?

There are three sites involved in the Target 5000 project. They are based at the Royal Victoria Eye and Ear Hospital, Dublin, the Mater Hospital, Dublin, and the Royal Victoria Hospital in Belfast. The research teams will receive the requests for genetic sequencing from us and will call you when they have an upcoming clinic. When you attend your appointment, there are a couple of different things that will happen. The appointment may take up to three or four hours.

- You will be asked to sign a consent form indicating that you are a voluntary participant in the project.
- You will be asked some questions about your condition, including onset of symptoms.
- You will also be asked about any family history of sight loss and if any family members are affected by similar or other sight loss conditions. This information is hugely important so that clinicians can try to determine inheritance patterns of conditions.
- You will be asked to give a blood sample. The blood samples will be sent directly to Trinity College Dublin (TCD) and held securely. DNA will be extracted from the blood samples in TCD. A portion of the DNA sample is kept in secure storage in TCD, and a portion is sent for next generation sequencing to an accredited laboratory. A raw, DNA sequence file will then be sent back to TCD for analysis.
- The clinician will perform a series of visual tests. This is very important because as well as finding out the genetic cause of the condition, we also want to compare this with what your current vision is like. You will find a list of these tests on page 25 of this booklet.

How long will it take to get my results?

It is impossible to predict how long it will take to find your causative mutation as this will differ greatly from person to person, depending on the gene involved. When the research team finds your mutation, they will contact you to set up an appointment. The causative mutation will be added to the patient registry in order to match the clinical assessment data with a molecular diagnosis. This data may be used in the future to identify potential eligible participants for clinical trials.

If you have any questions about any of the information above or would like to find out more about the Target 5000 project, please contact the Fighting Blindness research manager on 01 6789 004 or target5000@fightingblindness.ie.

I was really excited when I heard about the Target 5000 project. I often feel very helpless when it comes to my condition because there is no treatment and nothing that I can do to improve the outcome or even get an idea of how it will progress. Target 5000 is something proactive that I can do and that my family can get involved in as well. It makes me feel like I'm doing something useful that will help me find out more about my condition, but also help research that may lead to some form of treatment in the future.

Triona, Offaly

Retinal degeneration research is one of the most exciting and dynamic areas of current medical and scientific investigation. Until recently, there were no treatment options available for most of these conditions, but that has begun to change. I hope this guide gives an overview of how far we have come, as the number of therapies currently in research and development continues to grow.

Dr Maria Meehan
Research Manager, Fighting Blindness

Rare Inherited Conditions

Retinitis Pigmentosa
Choroideremia
Leber Congenital Amaurosis
Usher Syndrome
Stargardt Disease
Juvenile X-linked Retinoschisis
Leber Hereditary Optic Neuropathy
Best Disease
Cone Rod Dystrophies
Achromatopsia

Retinitis Pigmentosa

Retinitis pigmentosa (RP) refers to a group of inherited diseases that affect the photoreceptor (light sensing) cells that are responsible for capturing images from the visual field. These cells line the back of the eye in the region known as the retina. People with RP experience a gradual decline in their vision because the two types of photoreceptor cells - rod and cone cells - die. Rod cells are present throughout the retina, except for the very centre, and they help with night vision. Cone cells are also present throughout the retina, but are concentrated in the central region of the retina (the macula). They are useful for central (reading) vision, for colour vision and for side vision. In RP, the rod cells, and eventually the cone cells stop working, causing vision loss; however, many people with RP retain useful central vision well into middle age.

What are the symptoms of RP?

Rod cells are usually initially involved as previously mentioned and difficulty seeing in dim light, including transitioning from light to dark and vice versa, is one of the earliest symptoms experienced. There can be a very variable range in the onset of RP. Some people are diagnosed in childhood while others are not affected until they are adults. The condition is slowly degenerative, but the rate of progression and degree of visual loss can vary from person to person and even among affected members of the same family. It is therefore very difficult to predict what an individual's vision will be like at a specific time in the future. Both eyes are usually affected in a similar way.

What is the cause of RP and how is it inherited?

In Ireland, it is estimated that 1 in 4000 people have RP, which equates to approximately 1500 individuals. RP is one of the most complicated genetic conditions of all, and over 50 different genes have been identified to be causative for various forms of RP. There are various inheritance patterns for RP, including autosomal dominant (30-40%), autosomal recessive (50-60%) and X-linked (5-15%). Approximately 50% of RP patients will have a history of at least one other family members also being affected. 50% of patients will not have a positive family history. While their RP is still caused by a gene alteration, it might not be possible to determine the inheritance pattern in these patients. See previous section on inheritance patterns here on page 36.

The autosomal dominant form of disease tends to follow a milder course with maintenance of preserved vision well into late middle age. The X-linked form is the most severe and central vision may be lost by the third decade. RP is a genetic disease, but cases with no family history also commonly occur. If a family member is diagnosed with RP, it is strongly advised that other members of the family also have an eye exam by an eye doctor (ophthalmologist) who is specially trained to detect retinal diseases.

What treatments are available?

Maximising the remaining vision that an individual has is a crucial first step to take, and there are many new low vision aids including telescopic and magnifying lenses. The wide range of assistive technologies for people with visual impairments provides plenty of choice for users at all stages of sight loss, and this technology has also removed many barriers to education and employment.

There are, as of yet, no proven or effective cures for RP although research in this area has recently accelerated. The term RP represents an extremely varied number of diseases, as scientists have now identified more than 50 genes that can have mutations that cause RP and a number of these were discovered in Irish individuals by research performed in Trinity College, Dublin. It is likely that mutations in more than 100 different genes will eventually be identified in coming years.

Typically, each person with RP only has damage in one pair of genes, and gene therapy to replace defective genes by inserting healthy genes into the retina via harmless viruses has begun to be explored in clinical trials for a small number of RP genes. Scientists have also begun to treat animals with many other forms of RP with this approach and several more treatment trials in humans are expected to begin in the near future. Each of these hoped-for, new treatments will be specific for the gene responsible for the individual patient's form of RP. This is the reason why Fighting Blindness considers Target 5000, designed to identify the genes responsible for inherited retinal degenerations in Irish patients, including those with RP, to be so important.

Another research area currently being explored is the area of promising drug treatments that aim to preserve the function of the rod and cone photoreceptor cells, thereby keeping them alive for longer. Many of these drugs are "repurposed" drugs, which may have already been approved for a different disease, and are now being tested for their effectiveness in RP. It is estimated that as few as 5% of cone cells need to be preserved by such a treatment in order to have a huge impact on quality of life by the maintenance of a small but significant amount of central vision.

Gene therapy and drug therapies hold huge promise to treat individuals at an early to mid-stage of disease progression where there are still some viable rod and cone cells present. For individuals who may have lost a significant portion or all of their vision, there are other technologies that are being investigated, such as stem cell therapies and retinal implant technologies.

Stem cell technology holds great potential to replace retinal cells that have already died due to degeneration. Scientists are currently working on replacing two different cell types by stem cell therapy - retinal pigment epithelium (RPE) cells and photoreceptor cells. RPE cells are a special type of cell that support the photoreceptor cells, but are not responsible for "seeing", therefore it is hoped that replacement of RPE cells will help the retina function better, prevent further vision loss, and help nourish surviving retinal cells. This cell type would need to be replaced in time to help support a retina that is still working. Efforts at transplanting stem cell-derived photoreceptor cells are at an even earlier stage of research, but a number of recent animal studies have shown the potential to restore function in the eye, which may pave the way for human studies in the future.

Retinal implants are a form of biomedical technology currently being developed for retinitis pigmentosa. A number of these implants have shown success in delivering a form of artificial vision to individuals with total vision loss due to RP. When all or most of the photoreceptor cells have died, they can theoretically be replaced by an electronic microchip that brings a visual image to the remaining cells of the retina. These microchips electronically signal the remaining retinal cells which pass the signal down the optic

nerve for processing as a visual image by the brain. At the moment, these devices do not restore natural vision, but can help to restore mobility, by allowing an individual to see a difference in light and dark to the point where they can tell how to walk through a doorway.

Despite the lack of current treatments for RP, it is still very important to continue having regular general eye check-ups. This is because people with RP are still at risk for other kinds of eye problems that can affect the general population, and may be treatable. RP patients tend to develop cataracts at an earlier age than the non-RP population and can do very well from cataract surgery, although the visual outcome obviously depends on the severity of the retinal degeneration. Regular visits to your eye doctor can also make you aware of current advances as we learn more about RP.

Useful Links
RP Fighting Blindness www.rpfightingblindness.org.uk

Fighting Blindness is a key driver of vision research in Ireland. They have not only funded postgraduate and postdoctoral researchers in my group to advance vision research, but they have also enabled us to directly interact with patients, clinicians and pharma, thereby providing a multi-dimensional perspective on the vision research needs and potential in Ireland.

Dr Breandán Kennedy,
University College Dublin

Choroideremia

Choroideremia (alternative spelling: Choroideraemia) is a genetic condition that causes progressive vision loss mostly in men and is due to a degeneration of the specialised light-sensing photoreceptor cells that line the back of the eye. The vision loss due to choroideremia gets worse over time, eventually leading to blindness, but the rate of progression can vary between two individuals. Choroideremia is likely to be underdiagnosed as its symptoms are quite similar to a number of other retinal conditions such as retinitis pigmentosa. The distinctive appearances at the back of the eye and X-linked inheritance pattern help eye doctors to make the diagnosis.

What are the symptoms of Choroideremia?

Choroideremia causes damage to the network of blood vessels behind the retina that are known as the choroid. The choroid supplies oxygen and nutrients to support and nourish the retinal pigment epithelial (RPE) cells and the photoreceptor (rod and cone) cells. One of the earliest symptoms of the condition is difficulty seeing at night time, due to rod cell death because of a lack of nourishment from the choroid. Over time, the visual field narrows and progresses to tunnel vision and blindness commonly occurs in late adulthood.

What is the cause of Choroideremia and how is it inherited?

Choroideremia is a rare disease, estimated to affect approximately 1 in 50,000 people, although the exact prevalence in Ireland is currently unknown. Unlike some other retinal degenerations, such as retinitis pigmentosa, cases of choroideremia are due to mutations in just one gene, known as CHM. This gene makes an essential protein called REP-1, which is involved in escorting essential nutrients between cells in the back of the eye. However, about 20% of patients with a clinical diagnosis of Choroideremia have been found not to have a mutation in the CHM gene.

Choroideremia is genetically passed through families by an X-linked pattern of inheritance. The CHM gene is located on the X chromosome. Females have two X chromosomes, but generally only one of the chromosomes will carry a faulty copy of the gene and the other functioning copy will compensate. Therefore, females are carriers of the condition, but do not generally display the severe symptoms of the disease. In women, one or other of the two X chromosomes is randomly inactivated in every cell. Usually, in female carriers of X-linked disease genes, including CHM, this results in 50% of the retinal cells working on the altered CHM gene and the other 50% working on the normal copy of the CHM gene. These women will have very subtle, if any, symptoms of the disease. Inactivation, however, in some women may be skewed in favour of either the normal or the altered CHM gene copy. If greater than 50% of the normal CHM copy is inactivated the carrier female will have more in the way of symptoms. In rare, extreme cases of skewed inactivation the carrier female might be almost as severely affected as a male. Males only have one X chromosome and will become affected by the condition if he receives a faulty copy of the gene. Affected males cannot pass on the disease to their sons, because they pass on their Y chromosome. Men affected with Choroideremia must pass on the disease gene to all of their daughters, who then themselves become carriers of the gene.

See previous section on inheritance patterns here on page 36.

If a family member is diagnosed with choroideremia, it is strongly advised that other members of the family also have an eye exam by an eye doctor (ophthalmologist) who is specially trained to detect retinal diseases.

What treatments are available?

Maximising the remaining vision that an individual has is a crucial first step to take, and there are many new low vision aids including telescopic and magnifying lenses. The wide range of assistive technologies for people with visual impairments provides plenty of choice for users at all stages of sight loss, and this technology has also removed many barriers to education and employment.

There are no proven treatments for choroideremia although in recent years there have been momentous leaps made in clinical research and development. Over the past twenty years, researchers have identified the causative CHM gene, explored gene therapy in mouse models of disease and performed necessary safety tests of the treatment. This has culminated in the authorisation of a small gene therapy clinical trial, and more trials are expected in the near future. In these gene therapy trials, the researchers engineer a small, safe virus to deliver the correct version of the CHM gene into the light-sensing photoreceptor cells in the retina. The patient's retina is first detached and then the virus is injected underneath using a very fine needle. Early results from this trial have been positive, no safety issues have been reported and in some cases, gains in vision have been observed. However, it is still early days, and monitoring of the safety and effectiveness of this treatment will be a priority for the researchers over the coming years.

Useful links

Choroideremia Research Foundation www.choroideremia.org

Leber Congenital Amaurosis

Leber Congenital Amaurosis (LCA) is a rare genetic eye disease that appears at birth or in the first few months of life. The extent of vision loss varies from patient to patient, but can be quite severe (with little to no light perception). LCA is actually a term given to a group of diseases that are caused by mutations in at least 14 genes. The gene mutations lead to failure in function of the photoreceptor cells (rod and cones cells that receive light), ultimately causing cell degeneration. Given the severity of the condition, it is one of the most extensively researched inherited retinal disorders, and a number of clinical trials have begun recently.

What are the symptoms of LCA?

There are many different types of LCA, and the disease can present differently in different children. However, there are some basic symptoms that are often associated with LCA. These include nystagmus (involuntary jerky rhythmic eye movement), photophobia (sensitivity to light) and slow pupillary response to light. Eye-pressing and rubbing the eyes with a knuckle or finger can be common with babies and children who have very little vision. This can cause damage to the cornea (keratoconus) and lens and may result in a loss of fatty tissue around the eyes causing the eyes to look deep-set. The extent of degeneration depends on the type of LCA the child has and for some types of LCA the vision (or lack of vision) remains stable.

What is the cause of LCA and how is it inherited?

LCA is a very rare condition which is estimated to affect around 1 in 80,000 in the population. Forms of LCA are caused by a mutation in one of a number of genes that are important for retinal function and it is usually inherited in an autosomal recessive manner. However, there are rare incidences where the inheritance pattern may be autosomal dominant. See previous section on inheritance patterns here on page 36.

What treatments are available?

At present, there are no proven effective treatments for LCA. However a number of clinical trials have begun or are due to begin for some subtypes of the condition.
Gene therapy for a form of LCA known as LCA2 has begun to gather momentum in recent years, and a number of small clinical trials are currently underway. In the LCA2 clinical trials, gene replacement therapy involves engineering a “normal” copy of the RPE65 gene in the laboratory and injecting harmless viral particles containing the gene into the back of the eye to allowing integration of the gene into the DNA. Encouragingly, there have been no safety issues reported with these clinical trials thus far and improvements in vision have been observed. These trials are on-going, and more trials for other subtypes of LCA are planned to begin recruitment in the near future.

Promising human clinical trials investigating an oral drug are also underway in forms of LCA due to alterations in the RPE65 gene or the LRAT gene. These therapies aim to improve vision by bypassing the biochemical effects of lack of RPE65 or LRAT and thus “reawakening” dormant or sleeping retinal cells in order to allow the patient to see.

It is extraordinary that this very uncommon, and severe, inherited retinal degeneration is the subject of two different clinical trials, both of which have shown early evidence of success. This gives justifiable hope that less severe inherited retinal degenerations might also treatable in the foreseeable future.

Usher Syndrome

Usher syndrome refers to a group of genetic conditions that have both hearing loss and progressive deterioration in vision due to retinitis pigmentosa. While patients with retinitis pigmentosa do have a greater tendency to develop hearing difficulties as they age compared to the general population, the term Usher syndrome is reserved for patients where the hearing loss becomes obvious at a very early age. The vision loss aspect of the syndrome is due to a form of retinitis pigmentosa which affects the photoreceptor cells, and which are responsible for capturing images from the visual field. Usher syndrome causes a gradual decline in vision because two types of photoreceptor cells known as the rod and cone cells begin to degenerate and die. Usher syndrome is responsible for the majority of cases of deaf-blindness, but the rate of progression of vision loss can vary widely from person to person and even within members of the same family. Some people with Usher syndrome may also have problems with their balance.

What are the symptoms of Usher syndrome?

The major symptoms of Usher syndrome are hearing loss and an eye disorder called retinitis pigmentosa, or RP. The deafness is the first symptom to become apparent, usually from birth. There are broadly three different clinical types of Usher syndrome, type 1, type 2, and type 3. In Ireland, types 1 and 2 are the most common types. People with Usher type 1 develop profound deafness from birth and early childhood symptoms of RP. The deafness is generally so early in onset and so severe that hearing aids may not be of value, although cochlear implants may be beneficial, and patients fail to develop intelligible speech. Patients with Usher type 2 also have an early onset hearing loss but the deafness is less severe than in type 1 and thus the child will benefit from hearing aids and will develop intelligible speech. In type 2 Usher syndrome the features of RP usually become obvious during their teenage years. Usher type 3 is a very rare form of Usher and is generally found in people with their family origins in Finland.

What is the cause of Usher syndrome and how is it inherited?

The prevalence of Usher syndrome varies from country to country, but it is a rare condition affecting approximately 1 in 10,000 people. Usher syndrome is a genetic disease that occurs when there are mutations (defects) in genes that are important for the function of both photoreceptors in the retina and hair cells in the cochlea, or inner ear. So far, researchers have found 11 genes that are associated with the three main subtypes of the syndrome. Usher syndrome is always inherited in a recessive pattern. Patients with a combination of early-onset partial deafness and retinitis pigmentosa but due to alterations in the mitochondrial DNA do not fall into the category of Usher syndrome. See previous section on inheritance patterns here on page 36.

If a family member is diagnosed with Usher syndrome, it is strongly advised that other members of the family also have an eye exam by an eye doctor (ophthalmologist) who is specially trained to detect retinal diseases. As the deafness becomes obvious at a much earlier age than the RP in patients with Usher syndrome, it is particularly important that younger siblings with a hearing problem have a careful eye examination.

What treatments are available?

Current treatment focuses on helping an individual adapt to hearing and vision loss and maximising the vision and hearing that an individual has. This includes the use of hearing aids, assistive listening devices, cochlear implants, mobility training, and low vision services. The wide range of assistive technologies available provides plenty of choice for users at all stages of sight and hearing loss and this technology has also removed many barriers to education and employment.

Prospects for the development of effective Usher syndrome treatments have never been brighter. The syndrome is passed down through a recessive pattern of inheritance with only one pair of genes affected and is therefore a prime candidate for gene therapy. Gene therapy involves using harmless viruses to deliver and insert a healthy copy of the gene into the retina, thereby restoring function. This approach has led to exciting initial results in a number of other retinal diseases. Usher syndrome gene therapy is quite challenging as the genes affected tend to be extremely large in size and difficult to deliver. However, scientists are exploring other harmless viruses that have the ability to safely deliver these large genes. One trial is currently in the early stages of recruitment in the USA and France, and more trials are planned in the future.

Some forms of Usher syndrome are due to mutations known as “nonsense” mutations that lead to the incomplete and premature production of essential proteins. There are now new drugs in the very early stages of testing for a number of other rare genetic conditions due to nonsense gene mutations that may have the potential to stop the defective protein synthesis and produce the correct form of the protein. Neuroprotective agents that aim to preserve the function of the rod and cone photoreceptor cells for longer also hold huge potential for Usher syndrome, by maintaining a small, but significant amount of central vision.

Many of the therapies that are in development will not bring back the lost vision that occurs due to Usher syndrome, but they do have the potential to slow down or halt further degeneration, until other therapies, such as the exciting developments that have occurred in stem cell research, become available. Efforts at transplanting stem cell-derived photoreceptor cells are still at an early stage of research, but a number of recent animal studies have shown the potential to restore function in the eye, which may pave the way for human studies in the future.

Despite the lack of current treatments for Usher syndrome, general eye check-ups are important. This is because people with Usher syndrome are still at risk for other kinds of eye problems that can affect the general population, such as cataracts, and may be treatable. Regular visits to your eye doctor can also make you aware of current advances as we learn more about these conditions.

Useful Links

Deafblind Ireland www.deafblindireland.ie
The Anne Sullivan Foundation www.annesullivan.ie
Irish Deaf Society www.irishdeafsociety.ie
Usher Syndrome Coalition www.usher-syndrome.org
Sense www.sense.org.uk

Stargardt Disease

Stargardt disease is the most common form of inherited juvenile macular degeneration and affects the portion of the retina known as the macula. The macula is the central portion of the retina that contains photoreceptor cells known as cone cells that are responsible for central (reading) vision and for colour vision. Stargardt disease, also known as fundus flavimaculatus, is usually diagnosed in individuals under the age of 20 when decreased central vision is first noticed; for example a person may have difficulty seeing the board in class. The progression of visual loss varies hugely between individuals, but side or peripheral vision is usually preserved. This means that patients with Stargardt disease rarely have issues with independent mobility.

What are the symptoms of Stargardt disease?

Central vision is usually the first affected, and the first symptom is often difficulty reading. Blind spots can occur, and these may increase in size over time. The condition can be slowly degenerative and progressive, but it is very uncommon for someone with Stargardt disease to become completely blind. Both eyes are usually affected in a similar manner and colour vision may be affected in the later stages of disease. The rate of progression and degree of visual loss can vary from person to person and even among affected members of the same family. It is, therefore, very difficult to predict what an individual's vision will be like at a specific time in the future.

What is the cause of Stargardt disease and how is it inherited?

The prevalence of Stargardt disease worldwide is estimated to be 1 in 8,000 to 1 in 10,000 and in Ireland this equates to approximately 600-800 affected individuals. The majority of people with Stargardt disease have the recessive form of disease, involving mutations in the ABCA4 gene, which provides instructions to make the ABCA4 protein. If there is a faulty ABCA4 gene it leads to the build-up of a toxic waste product known as A2E in the retinal pigment epithelium and can lead to macular degeneration and progressive loss of vision.

A very rare form of Stargardt disease may be caused by mutations in the ELOVL4 gene and follows an autosomal dominant form of inheritance. Mutations in the ELOVL4 gene can make dysfunctional ELOVL4 protein clumps that can interfere with photoreceptor cell functions leading to cell death. See previous section on inheritance patterns here on page 36.

If a family member is diagnosed with Stargardt disease, it is strongly advised that other members of the family also have an eye exam by an eye doctor (ophthalmologist) who is specially trained to detect retinal diseases.

What treatments are available?

At present, there are no effective treatments for Stargardt disease, but there is research to suggest that UV sunlight can increase the toxicity of the waste products accumulating in the retina. Therefore, it is recommended that people with Stargardt disease wear UV-screening sunglasses when out in direct sunlight. Recent evidence also suggests that taking extra vitamin A, such as in a vitamin supplement, may have a negative effect on the condition and should be avoided.

Gene therapy is currently being explored for the recessive form of Stargardt disease caused by ABCA4 mutations. The idea behind gene therapy is that a "normal" copy of the ABCA4 gene can be engineered in the lab. This can then be injected into the eye of an affected individual, delivering the correct copy of the gene and therefore stopping the degeneration of the sight of the individual. This approach is currently in the early stages of a clinical trial in the USA and France in order to find out if this is a safe approach. If this gene therapy is found to be safe, the trial will move on to the next stage which will be to test how effective this experimental treatment is.

Stem cells are amazing cells that are produced in the body and have the remarkable potential to develop into many different cell types in the body during early life and growth. A number of groups worldwide are currently manipulating stem cells from various origins in order to produce retinal pigment epithelial cells (RPE) and these cells have been injected into a number of patients. Thus far, these cells have proven to be safe and well tolerated. The transplantation of these functional cells into patients may prevent the death of the remaining photoreceptors and may, therefore, help Stargardt patients avoid blindness. These early stage clinical trials are currently on-going. Efforts at transplanting stem cell-derived photoreceptor cells are at an even earlier stage of research, but a number of recent animal studies have shown the potential to restore function in the eye, which may pave the way for human studies in the future.

Another interesting approach that is currently being studied as a therapy involves research into a modified form of vitamin A called deuterated vitamin A. The researchers hope that this may help slow the accumulation of A2E by blocking its formation downstream in the visual cycle. They are currently testing the safety of this approach. Please note however that recent evidence suggests that taking extra "normal" vitamin A, such as in a vitamin supplement from a health shop, may have a negative effect on the condition and should be avoided as this can increase toxic levels of A2E.

Despite the lack of current treatments for Stargardt disease, general eye check-ups are important. This is because people with Stargardt disease are still at risk for other kinds of eye problems that can affect the general population and may be treatable. Regular visits to your eye doctor can also make you aware of current advances and new treatments as we learn more about the condition.

Juvenile X-linked Retinoschisis

Juvenile X-linked retinoschisis is a rare genetic disease of the retina and affects primarily boys and young men. Retinoschisis is a condition in which an area of the retina (the tissue lining the inside of the back of the eye that transmits visual signals to the optic nerve and brain) has separated into two layers. The part of the retina that is affected by retinoschisis will have poorer vision, however very few people with retinoschisis lose all of their vision.

What are the symptoms of retinoschisis?

Affected boys are usually identified in primary school, but occasionally are identified as young infants. Most boys with retinoschisis present with a mild decrease in central vision in primary school that may be subtle and not perceptible. They may continue to lose vision into their teens. Once they are adults, their vision often stabilises until they are in their 50s or 60s. Retinoschisis patients are more susceptible to retinal detachment and eye haemorrhage (bleeding) than other people and they should have regular examinations with an eye doctor. When detected early, a complicating retinal detachment can be treated surgically.

What is the cause of retinoschisis and how is it inherited?

The exact prevalence of retinoschisis is currently unknown, but it is thought to affect between one in 5,000 to 25,000 people, and is therefore a rare condition. X-linked retinoschisis is usually caused by mutations (defects) in the RS1 (retinoschisin 1) gene located as the name suggests on the X chromosome. Men have only one X chromosome, while women have two. Therefore, because women almost always have another functioning X chromosome, they typically retain normal vision, even as carriers. However, in rare circumstances, due to the phenomenon of 'non-random X chromosme inactivation' some female carriers may have symptoms. Men, on the other hand, will develop suboptimal vision if they have an affected X chromosome. Affected males cannot pass on the disease to their sons, because they pass on their Y chromosome. Men affected with retinoschisis must pass on the disease gene to all of their daughters who become carriers of the condition.

What treatments are available?

Maximising the vision that an individual has remaining is a crucial first step to take, and there are many new low vision aids including telescopic and magnifying lenses.

Currently, there are no medical or surgical treatments available for retinoschisis. Glasses may improve the overall quality of vision in a patient with retinoschisis who is also nearsighted or farsighted, but will not repair the nerve tissue damage from the retinoschisis.

In 1997, researchers identified mutations in the RS1 gene on the X chromosome that cause retinoschisis. Scientists then studied the gene to determine its function in the retina and this work has greatly enhanced efforts to develop treatments for this condition. A number of groups worldwide are now working on developing gene therapies for retinoschisis. These innovative therapies aim to deliver healthy copies of the RS1 gene by a non-toxic virus, therefore replacing defective copies at the back of the eye. This type of gene therapy has been shown to be safe in other conditions, and it is hoped that small clinical trials in order to determine safety of this approach in retinoschisis will begin soon.

General eye check-ups are important for people with retinoschisis as these men and boys are still at risk for other kinds of eye problems that can affect the general population and may be treatable. They are also more vulnerable to retinal detachments and haemorrhages. Regular visits to your eye doctor can also make you aware of current advances as we learn more about retinoschisis.

Leber Hereditary Optic Neuropathy

Leber hereditary optic neuropathy (LHON) is a genetic disease that leads to sudden vision loss during young adult life. Men are more likely to be affected than women. LHON is a disorder caused by mutations in the genetic code of the mitochondria which are little subunits that reside within the cell. Mitochondria are also known as the “powerhouses of the cell” as they constantly convert energy locked in our food into energy that the cell can use.

Our eyes are our most energy hungry organs and a lack of energy production can lead to degeneration and death of retinal ganglion cells (RGCs) which are the nerve cells that communicate visual information to the brain. Loss of these cells leads to subsequent degeneration of the optic nerve and visual loss. However, it is worth noting that a significant percentage of people who possess a mutation that causes LHON do not develop any features of the disorder.

Loss of vision due to LHON does not cause any eye pain, but it is quite an alarming experience as the loss of central vision presents suddenly and can progress quite quickly, leaving only peripheral vision. This means that the majority of people with LHON retain independent mobility but cannot focus on anything straight ahead or see fine detail.

What are the symptoms of LHON?

Affected individuals do not usually present any symptoms until they develop visual blurring affecting their central vision. These vision problems may begin in one eye or both simultaneously. If one eye is affected, then similar symptoms appear in the other eye on average eight weeks later.

Over time, the vision in both eyes worsens with a severe loss of sharpness and a fading of colour vision. The vision loss mainly affects central vision, which is needed for tasks such as reading, driving and recognising faces. In a small percentage of cases, the central vision loss can improve; but in most cases loss of vision is permanent.

The severity of symptoms may vary from one affected individual to another, even within the same family due to a ‘dosage’ effect. This is due to the fact that we have many mitochondria in each cell. In one individual, if only a small proportion of mitochondria in each cell have the mutation, symptoms will be mild. In another individual, if a higher proportion of mitochondria in each cell carry the mutation, symptoms will be more severe.

What is the cause of LHON and how is it inherited?

LHON follows a mitochondrial pattern of inheritance, which is also known as maternal inheritance. Only egg cells and not sperm cells contribute mitochondria to a developing embryo, therefore only females can pass mitochondrial conditions to their children. Fathers affected by LHON or carrying LHON mutations do not pass the condition to their children.

Often, people who develop LHON have no family history of the condition. However, it is currently impossible to predict which members of a family who carry a mutation will eventually develop vision loss. More than 50% of men and more than 85% of women with a mitochondrial mutation will never experience vision loss. LHON is a very rare condition. Exact prevalence is unknown in Ireland, but it is thought to affect between 1 in 30,000 to 1 in 50,000 individuals worldwide. Research has revealed that three particular mutations in mitochondrial genes account for between 85% – 90% of cases of LHON.

What treatments are available?

Currently, there are no approved treatments or cures for LHON. There is strong evidence that environmental factors such as smoking and excessive alcohol consumption are linked to why some susceptible people develop the condition and others do not. Therefore many actions that contribute to a healthy lifestyle should be adopted by those at risk. A number of new therapies are also in development for the treatment of LHON, including pharmaceutical compounds and gene therapies.

There is a growing body of evidence to suggest that idebenone, an antioxidant compound initially developed for the treatment of Alzheimer's disease, may be effective in the treatment of LHON. Studies have found that idebenone is effective during the earliest phase of symptoms and protects from further retinal ganglion cell loss. Other antioxidants are currently being examined for their protective effects on the retina.

A number of research teams are investigating gene based therapies for the treatment of LHON including our own dedicated researchers in Trinity College, Dublin. Gene therapies that target the cell nucleus have been successfully employed in other retinal conditions but progress in LHON has been slower as there is a need to deliver such a therapy targeted to the mitochondria, of which there may be hundreds or thousands within a single cell. However, many of these barriers have now been overcome and progress in LHON gene therapy will be eagerly monitored over the coming years.

Useful Links
LHON Society www.lhonsociety.org

Best Disease

Best disease, also known as vitelliform macular dystrophy, is an inherited form of retinal degeneration affecting the portion of the retina known as the macula. The macula is the central part of the retina containing the photoreceptor cells known as cone cells that are responsible for fine visual detail and colour perception. Best disease is usually diagnosed during the teenage years, but vision does not generally deteriorate until later in life. The progression of visual loss varies between individuals but side or peripheral vision usually remains unaffected. Therefore, people with Best disease do not generally have issues with independent mobility.

What are the symptoms of Best disease?

The first symptoms of Best disease can vary from person to person but always involves the central vision. In the initial stages, a fatty yellow pigment builds up in the cells underneath the macula. Overtime, this abnormal accumulation of this substance can damage the cone cells located in the macula, leading to a blurring or distortion of central vision. Best disease generally doesn't affect peripheral or side vision. It does not always affect both eyes equally and clearer vision is sometimes retained in one eye.

What is the cause of Best disease and how is it inherited?

Best disease is a genetic disease and is caused by mutations in the BEST1 gene which produces the protein Bestrophin-1. Best disease is passed down through families by an autosomal dominant pattern of inheritance. In this pattern of inheritance, an affected person has a mutated BEST1 gene paired with a normal copy of the BEST1 gene. When the affected person has children with an unaffected partner, there is a 50 percent chance that the affected parent will pass the mutated BEST1 gene to each child. The unaffected partner will only pass normal copies of BEST1 genes. A child who does not have a mutated BEST1 gene will not have the disease and cannot then pass the disease to his or her children. Owing to the variable expression of the BEST1 mutation some people who have the mutation may have very mild, or in rare cases no, symptoms. More information about patterns of inheritance can be found on page 36.

What treatments are available?

Currently, there is no treatment for Best's disease. Genetic research identified the BEST1 gene as causative for Best disease in 1998 and researchers are now working on understanding the function of this gene in the retina. Recently, there have been encouraging gene therapy studies in preclinical models of Best disease and these findings mark the first clear steps to developing a therapy that could prevent vision loss. Using this approach, which has proven safe in other retinal conditions, researchers engineer small, safe viruses to deliver the correct version of the BEST1 gene to the retina.

No matter what your level of sight loss, we are here to help and provide any support you or your family may need. We offer a variety of services and invite you to get in touch if there is anything that you feel may be of benefit to you.

Cone-Rod Dystrophies

Cone-rod dystrophies refer to a group of inherited diseases that affect the photoreceptor (light sensing) cells that are responsible for capturing images from the visual field. These cells line the back of the eye in the region known as the retina. Cone cells are present throughout the retina, but they are concentrated in the central region of the retina (the macula) and they are useful for central (reading) vision and for side vision. Rod cells are present throughout the retina except for the very centre and they help with night vision. In contrast to typical retinitis pigmentosa (known as the rod-cone dystrophies) which results from the loss of rod cells and later the cone cells, cone-rod dystrophies reflect the opposite sequence of events, where cone cells are primarily first affected with later loss of rods.

What are the symptoms of cone rod dystrophy?

The cone cells are initially involved as previously mentioned and difficulty with the clarity of vision, colour vision problems and light sensitivity can be some of the earliest symptoms experienced. This is followed by a progressive loss of rod cells, which leads to night blindness and loss of side vision. The age of onset, progression and severity of cone-rod dystrophies can vary greatly from one person to another, even among individuals with the same type of cone-rod dystrophy. It is therefore very difficult to predict what an individual's vision will be like at a specific time in the future. Some forms of cone-rod dystrophy are inherited; other forms appear to occur spontaneously for no apparent reason (sporadically).

Cone-rod dystrophies have many similarities to retinitis pigmentosa, and like RP they can follow varied inheritance patterns, including autosomal dominant, autosomal recessive, and X-linked. A comprehensive explanation of inheritance patterns can be found on page 36.

What treatments are available?

Maximising the vision that an individual has remaining is a crucial first step to take, and there are many new low vision aids including telescopic and magnifying lenses providing plenty of choice for users at all stages of sight loss and this technology has also removed many barriers to education and employment.

There are, as of yet, no proven or effective cures for cone-rod dystrophies, however scientists have identified more than 20 genes that can have mutations that can cause these conditions and it is likely that many more mutations in many more genes will be identified in the coming years. Many future treatments will rely on identification of these gene defects. This is the reason why Fighting Blindness considers Target 5000, designed to identify the genes responsible for inherited retinal degenerations in Irish patients, including those with cone-rod dystrophies, to be so important.

Despite the lack of current treatments for cone-rod dystrophies, general eye check-ups are important, because people with these conditions are still at risk for other kinds of eye problems that can affect the general population and may be treatable. Patients with cone-rod dystrophies tend to develop cataracts at an earlier age than the overall population. Regular visits to your eye doctor can also make you aware of current advances as we learn more about these conditions.

Sight loss is a life changing experience but not a life ending one. We grow and evolve so that sight loss informs but does not have to determine who we are or how we live our lives. I cherish the opportunity to walk that journey of discovery with every person who seeks my help.

John Delany, Insight Counselling Service

Achromatopsia

Achromatopsia is a rare hereditary vision disorder affecting the cone photoreceptor cells, resulting in an absence of colour vision along with additional visual problems. There are two main types of cells in the retina responsible for capturing the visual field; the rod cells and the cone cells. We use our rod cells at night time and in low light but they are not sensitive to colour and do not provide detailed vision. We use our cone cells in bright light, and they are responsible for our colour vision and also for our central, reading vision. Genetic changes or mutations in genes that function in cone cells are responsible for achromatopsia. Individuals with achromatopsia have reduced visual acuity and are completely or almost fully colour blind; however the condition is not progressive and it does not lead to blindness.

What are the symptoms of achromatopsia?

The condition is often first noticed in a young child by their parents, as children with achromatopsia may dislike bright lights and often avoid the daylight (known as photophobia). Nystagmus is another symptom of the condition where their eyes may involuntary move and "dance". Judging from their behaviour some parents may notice that their child's vision may be reduced or blurred. However, most children with achromatopsia have no problem with mobility or getting around.

What is the cause of achromatopsia and how is it inherited?

To date, mutations in one of five genes are known to cause achromatopsia. The condition is inherited in an autosomal recessive manner, which means that an affected individual inherits a mutated copy of an achromatopsia-linked gene from both parents. Most often, the parents of an individual with achromatopsia each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. See page 36 for more information about inheritance patterns.

What treatments are available?

The vision of people with achromatopsia decreases as the levels of light increase. In regular home lighting indoors or outdoors just after dawn or just before dusk, some people with achromatopsia adapt to their reduced level of visual function without resorting to tinted lenses. Instead, they use visual strategies such as squinting or shielding their eyes or they position themselves in favourable light. Others sometimes wear medium tinted lenses in such settings. However, in full sunlight outdoors or in very bright indoor spaces, almost all people with achromatopsia use very dark tinted lenses in order to function with a reasonable amount of vision, since they do not possess functioning cone photoreceptors needed in order to see well in these types of settings. Two of the most common genes linked to the condition (CNGB3 and CNGA3) account for 75% of cases of achromatopsia, making this condition potentially amenable to gene therapy. Based on a number of successful results in animal models of achromatopsia, a number of groups are in preparation for human gene therapy clinical trials. In these trials it is planned to deliver a "normal" copy of the mutated gene back to retina, in theory restoring cone function and visual function.

Fighting Blindness has helped my wife immensely by providing her with confidence and enthusiasm that great work is being done to help people with many different sight conditions including her own. Providing her with regular updates on new research, different support groups and new advancements in the fight against sight loss helps her overcome the challenges she faces every day and gives her hope for the future.

Michéal, Donegal

Age-related macular degeneration is a much talked about eye condition in the present day, but when I was diagnosed, the condition was unknown to me. Now I am a member of Fighting Blindness, and through their meetings and newsletters, I learn of the progress being made in the quest for suitable treatments for the various stages of AMD. As a result, I remain optimistic, even at my age, that some degree of improvement in my situation may soon be possible. Since my diagnosis, new doors have opened and I have made new friends. I have learned to adjust to my life with AMD and today, I am glad to say, I lead a happy and contented life.

Joe, Dublin

Other Conditions

Age-related Macular Degeneration
Diabetes Related Sight Loss
Sight Loss as Part of a Syndrome

Age-related Macular Degeneration

Age-related macular degeneration (AMD) is a disease that causes the gradual loss of sight causing blurring or loss of central vision. This is often due to a destruction of the macula, a yellow pigmented structure at the back of the eye that is responsible for our detailed colour vision. The severity of the disease depends on each person and on how quickly it is detected. AMD is a chronic disease – it cannot be cured and in many patients sight cannot be restored after it is lost. However certain forms of the disease can be treated. Early detection is important to potentially stop the spread of the disease and to protect your sight.

There are two forms of AMD, Early and Late. In Early AMD the signs that the retina is being damaged are only visible to your eye care practitioner (optometrist or eye doctor). At this stage the damage does not affect sight and people are unaware of the condition. This highlights the importance of regular eye examinations to detect AMD in its early stages.

Some people progress from Early to Late AMD, where the condition causes loss of vision. There are two forms of Late AMD, Dry and Wet AMD. The wet form is more severe and vision degenerates more rapidly, however this form is less common. Abnormal blood vessels grow under the macula which bleed and leak fluid, this causes central vision to become damaged or distorted. This is called choroidal neovascularization (CNV). The dry form is more common (around 85% of people with AMD have the dry form) but it is less severe and vision degenerates over a longer period of time. Dry AMD is caused when deposits, called ‘drusen’, form at the macula. Only your eye care professional can tell you which form you may have.

Although sight loss caused by AMD can cause difficulty doing everyday tasks like driving, reading and watching TV, AMD rarely causes total blindness.

What are the symptoms of AMD?

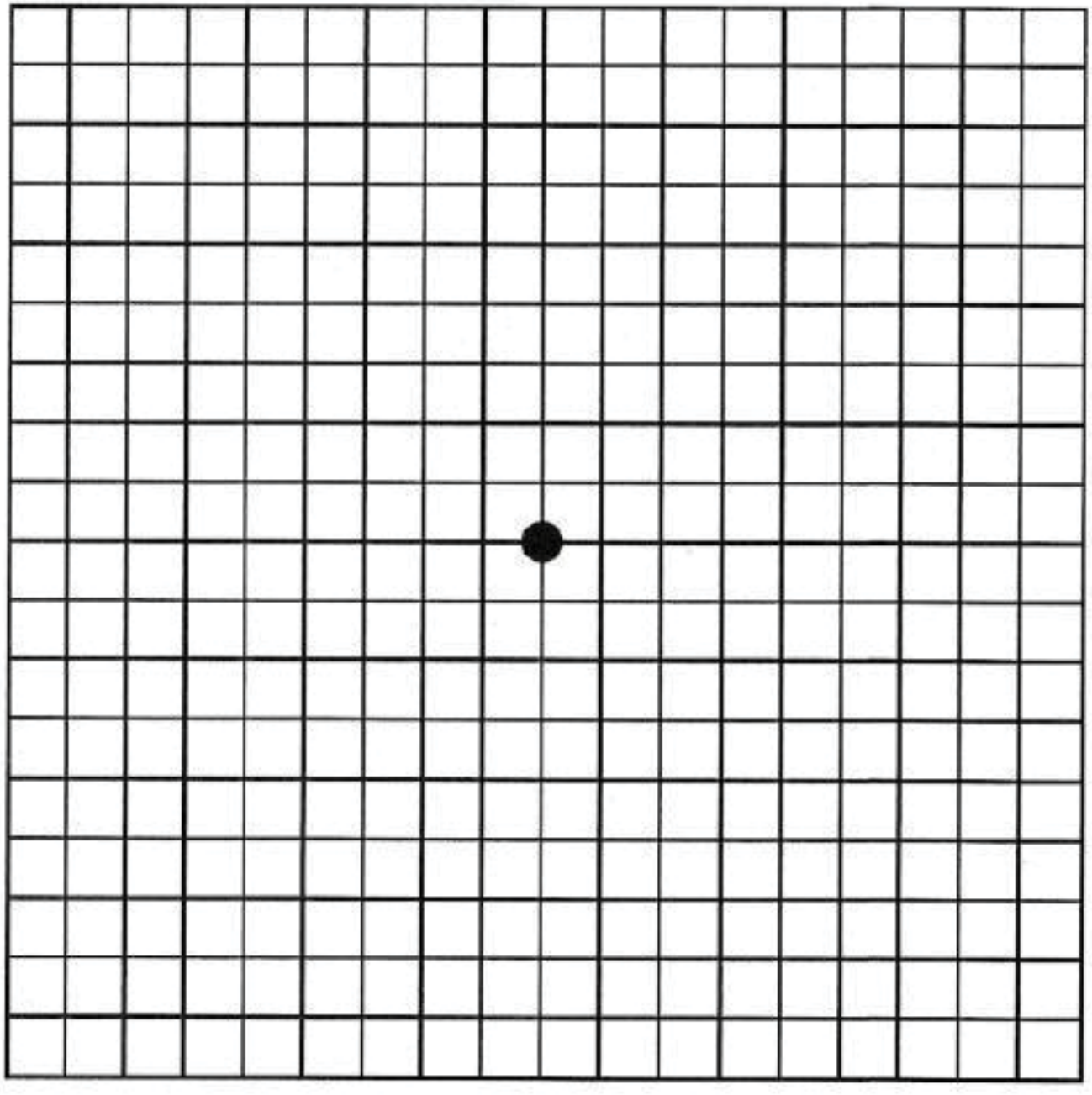
Key early symptoms of AMD include a blurring of central vision and straight lines appearing distorted, for example door-frames and steps. Everyday activities such as driving, watching TV, and even recognising faces can become seriously affected over time. It is important to have your eyes tested every two years. If you notice any change in your vision, especially blurring, see your optometrist or doctor right away. Today, many optometrists can take a photograph of the back of your eye to detect irregularities. They may also shine a small light into the back of your eye to detect presence of drusen, a characteristic of dry AMD.

One easy at-home test for AMD is the Amsler Grid.

How to test with the Amsler Grid

- Hold the grid at reading distance, about 12 inches (30cm) away from your face.
- If you wear reading glasses, leave them on. Do not take the test while wearing varifocal or distance glasses.
- Cover one eye and focus on the centre dot.
- Make sure you can see all four corners of the grid.
- If the lines appear missing or wavy, you may have AMD. Contact your doctor immediately.

Remember, even if the grid looks normal, you should still attend regular eye exams for early detection of AMD.



What is the cause of AMD?

The exact cause of AMD is unknown, but over the past 20 years, many risk factors for AMD have been discovered. Researchers know that certain genes cause AMD, but they don't know what triggers the gene. While AMD can be inherited, many lifestyle choices can make progression of the disease worse.

You may be at risk of developing AMD if you are over the age of 50, have a family history of AMD, smoke and if you are overweight or have a poor diet. Other factors include having fair skin and light eyes and having a history of cataracts. Studies have shown that women are more likely to develop AMD.

There are simple steps you can take today to help save your sight. These include eating a balanced vegetable rich diet, exercising regularly and quitting smoking. Many of these are part of living a healthy lifestyle, so your heart and lungs will thank you too.

What treatments are available?

If your optometrist detects something wrong with your eye or suspects you have AMD, he or she will refer you to an ophthalmologist. This person will be able to medically treat your eyes and talk to you about the best course of action for your particular condition. Your eye care practitioner will suggest lifestyle changes that will help slow the progression of AMD, such as stopping smoking and eating a healthy diet. Vitamin supplements may also be recommended.

If Wet AMD is suspected, you may have a test called Fluoroscein Angiography. A special dye is injected into your arm and carried through your bloodstream. As it passes through the blood vessels in your eye, doctors can detect the severity of the leaking and bleeding. If you have Wet AMD, a treatment of anti-VEGF therapy may be recommended to treat the damaged blood vessels in your eye. The success of this therapy depends on early detection and treatment before irreversible scarring and damage occurs.

Internationally, researchers are trying to understand why some people get AMD and others do not. While we understand some of the risk factors and lifestyle choices that may lead to the disease, researchers are also investigating the role of the immune system in the disease progression. Researchers are also designing ways to deliver medication to the eye that are less invasive methods than current methods. Another key area of research is looking at ways of preventing the early stages of macular degeneration, when natural cell waste materials build up in the retina. This leads to toxic chemicals forming, which cause retinal cells to die. Drugs are being trialled to see if they can slow the buildup of the toxins. Neuroprotective drugs are also being investigated to see if they can protect the cells of the retina.

For people living with AMD, general eye check-ups are extremely important, because these individuals are still at risk for other kinds of eye problems that can affect the general population and may be treatable. Regular visits to your eye doctor can also make you aware of current advances as we learn more about treating these prevalent diseases.

Useful Links

Macular Society www.macularsociety.org
MIST (Macular Impairment Support and Togetherness) T 01 269 1921

The day after finding out I had Usher Syndrome, I contacted Fighting Blindness. It was the best thing I ever did, because this organisation has truly been and always is a beacon of hope for me through its dedication to initiating, promoting and funding research into retinal degenerative diseases. I have gained so much from being actively involved with Fighting Blindness, and have made many wonderful friends, who are affected by retinal degenerative diseases. It helps to ease the isolation and loneliness one can feel when learning to cope with sight deterioration. Most importantly, there is a great comfort knowing that Fighting Blindness are committed to finding a cure for blindness.

Carol, Dublin

Diabetes Related Sight Loss

Diabetes is a disease that occurs when the pancreas does not secrete enough insulin or the body is unable to process it properly. Insulin is the hormone that regulates the level of sugar (glucose) in the blood.

The effect of diabetes on the eye is called diabetic retinopathy. Diabetic retinopathy is a common complication of diabetes, it may not have any symptoms or may not affect sight in the early stages but as the condition progresses eventually the sight will be affected. When the condition is caught early, treatment is effective at reducing or preventing damage to sight.

Diabetic related sight loss is the most common form of blindness in people of working age in Ireland. In about 10% of cases, diabetic macular oedema (DME) may occur where blood vessels leak their contents into the macular region of the retina and this may cause a more rapid form of vision loss.

What are the symptoms of diabetic retinopathy?

The earliest phase of diabetic retinopathy is known as 'background diabetic retinopathy'. Often there are no symptoms in the early stages of the disease, nor is there any pain. In this phase, the arteries in the retina become weakened and leak, forming small haemorrhages. These leaking vessels often lead to swelling or oedema in the retina. As the disease progresses, some blood vessels that nourish the retina become blocked, over time worsening and depriving several areas of the retina with their blood supply.

In advanced diabetic retinopathy the signals sent by the retina for nourishment trigger the growth of new blood vessels. This condition is called proliferative retinopathy. These new blood vessels are abnormal and fragile. They grow along the retina and along the surface of the clear gel that fills the inside of the eye. By themselves, these blood vessels do not cause symptoms or vision loss. However, they have thin, fragile walls. If they leak blood, severe vision loss and even blindness can result.

A condition known as diabetic macular oedema occurs when blood leaks into the centre of the retina, known as the macula, the part of the eye where sharp, straight-ahead vision occurs. The fluid makes the macula swell, blurring vision. This can occur at any stage of diabetic retinopathy, although it is more likely to occur as the disease progresses.

The good news is that by regular and effective retina screening, diabetic retinopathy can be caught early and effectively treated. The national diabetic retina screening programme for diabetic retinopathy (Diabetic RetinaScreen) has been rolled out nationwide for everyone over the age of 12 who is affected by diabetes in Ireland. If you have diabetes it is extremely important that you reply to the letter you have received in order to express your interest in taking part in the eye screening. More information is available at www.diabeticretinascreen.ie, or on 1890 45 45 55.

What treatments are available?

Prevention of diabetic retinopathy is the most important step to take for anyone with diabetes. Researchers have found that diabetic patients who are able to maintain appropriate blood sugar and blood pressure levels have fewer eye problems than those with poor control. Diet and exercise play important roles in the overall health of people with diabetes.

People with diabetes can also greatly reduce the possibilities of eye complications by going to their routine examinations with an eye doctor and taking part in the national screening programme. Many problems can be treated with much greater success when caught early.

Diabetic retinopathy is treated in many ways depending on the stage of the disease and the specific problem that requires attention. The doctor relies on several tests to monitor the progression of the disease and to make decisions for the appropriate treatment. Laser eye surgery called pan retinal photocoagulation (PRP) is one treatment choice to prevent the blood vessels from leaking, or to get rid of the growth of abnormal, fragile vessels. A new class of drugs has recently become available to treat macular oedema, and they are often used in conjunction with the laser therapy. These are anti-VEGF (Vascular Endothelial Growth Factor) drugs and they target the substance in the body which is responsible for the development of blood vessels. In diabetic macular oedema, too much VEGF is produced in the eye, and these drugs block the production of these new, abnormal vessels.

Vitrectomy is another surgery commonly needed for diabetic patients who suffer a vitreous haemorrhage (bleeding in the gel-like substance that fills the centre of the eye). During a vitrectomy, the retina surgeon carefully removes blood, fibrous tissue and vitreous from the eye, relieving traction on the retina and preventing retinal detachment. If retinal detachments or tears occur, they are often sealed with laser surgery. Retinal detachment requires surgical treatment to reattach the retina to the back of the eye. The prognosis for visual recovery is dependent on the severity of the detachment.

Exciting research for diabetes and diabetic retinopathy is ongoing. Irish researchers from NUI Galway and Queen's University Belfast are part of an international collaboration who are assessing if stem cells derived from bone marrow can control glucose levels and stop some of the damage caused by six diabetic complications including diabetic retinopathy. Fighting Blindness supported researchers in UCD and the Mater Hospital are also designing tools that can detect, treat and prevent vision loss in people with diabetes. They are studying the molecular basis of diabetic retinopathy and they have discovered that there are resident populations of cells within the eye that can be manipulated in order to promote repair.

Useful Links

Diabetic RetinaScreen – The National Diabetic Retinal Screening Programme www.diabeticretinascreen.ie
Diabetes Ireland www.diabetes.ie

Retinal Degeneration as Part of a Syndrome

The eye is a complex part of the body and as a result there are also many different syndromes that sight loss may form a part of. Unfortunately we are not always able to produce detailed information for each of these syndromes, some of which are listed below.

- Alström Syndrome
- Bardet-Biedl Syndrome
- Wolfram Syndrome
- Joubert Syndrome
- Mainzer –Saldino Syndrome
- Stickler Syndrome

The Genetic and Rare Disorders Organisation (GRDO) provides a strong voice for voluntary groups representing people with or at risk of developing genetic or other rare disorders in order to achieve better support and services.

They can be contacted at info@grdo.ie. Please see www.grdo.ie for more information or call Fighting Blindness on 01 6789 004 and we can put you in touch with the organisation.

Having three of my children diagnosed with a vision impairment, the help and support of Fighting Blindness has been immense and their continued great work gives us real hope for a cure in the future.
Anne, Tipperary

When my daughter was diagnosed with retinitis pigmentosa at 23 we didn't know anything about the condition and were very overwhelmed. The support given to our family by Fighting Blindness was invaluable. A guide like this would have been very useful and I know that anyone facing a diagnosis today will find it really helpful.

Eileen, Cork

Connect

Connect with Fighting Blindness
How to Support Our Work

Connect with Fighting Blindness

There are lots of ways in which you can connect with Fighting Blindness. We welcome you to become a member and receive regular updates. You can also attend some of our events and information evenings. There are opportunities to work with us in advocacy and education to raise awareness about retinal conditions and their impact. You can also get involved in our fundraising and community activities. We would love to hear from you. Below, you will find some further detail on how you can get involved in the organisation.

Membership

As a patient-led organisation, our members are vital to our work. Membership is open to anyone with an interest in the organisation, including people with sight loss and their families, supporters and fundraisers, medical professionals, researchers and the general public. By becoming a member, you will receive an invitation to the Annual General Meeting, at which you will have voting rights, along with the opportunity to meet the staff and board, and contribute to the work of Fighting Blindness. You will also be invited to the Public Engagement Day of the annual Retina Conference, where you will hear the latest developments in retinal research in Ireland and globally. We will keep you regularly updated through our quarterly Visionaries newsletter. Membership is renewable on a yearly basis.

Target 5000

Target 5000 is a research project, led by Fighting Blindness. It aims to discover the specific gene abnormality for each individual who has an inherited retinal condition. You can discover more about Target 5000 on page 41 of this guide, or by contacting our office.

Visionaries Newsletter

We publish the Visionaries newsletter quarterly. It is available in printed format, as an ezine and can be downloaded from our website. Visionaries contains updates on research projects that we are funding as well as international advances in retinal research and clinical trial development. It also provides information about our counselling and support service and highlights activities in advocacy and patient empowerment. Further, it will keep you informed about our fundraising activities and tell you about the work of our many busy and inspiring supporters around the country.

Social Media

Social media is a great way to stay connected with what we are doing in short bulletins. We update our Facebook and Twitter daily with news about everything from local community events to international research.

Retina Conference

The Retina conference brings together top international scientists, Irish researchers and clinicians, and patient representatives who are involved in the global effort to develop treatments and cures for conditions that lead to sight loss. Since 2000, we have used the meeting as an opportunity for researchers and clinicians to learn from one another, by sharing the latest developments in the field. It also helps them to form links and collaborations that will accelerate the global fight to cure blindness. The conference takes place over two days. The first day is the Science Meeting, designed for a scientific and clinical audience where global advances in research and clinical trial progress will be

discussed. The second day is a Public Engagement Day and is designed for patients, family members and medical professionals to inform them about the work happening around the world.

The Retina conference takes place in November each year. Full details, including reports from previous years, can be found on www.retina.ie.

Fundraising Events and Activities

Fighting Blindness holds many varied fundraising activities throughout the year to help generate the vital funds needed to sustain our research and work. You can get involved in treks, runs, community events, bucket collections and anything else you can imagine! For more information about any of our events, or to discuss planning an event of your own, email fundraising@fightingblindness.ie.

Advocacy

We are very involved in patient empowerment and are working at the highest levels to ensure that the voice of patients is front and centre of any decision made about them. Particularly significant, current activities in this area include our position as co-chair in the development of a National Strategy for Vision and as part of the steering committee, driving the development and implementation of a National Rare Disease Plan. You can find much more detail about this work on our website. We would love to hear from you if you are interested in getting involved in this area of our work, by joining a discussion group or committee that is driving the development or by becoming a patient advocate.

Insight Counselling Service

Insight is a national support service from Fighting Blindness. It offers a wide variety of opportunities to support people with sight loss and also their families and friends. Services include individual therapy sessions, family and spousal sessions, support groups, a telephone helpline and hospital supports, amongst others. Full details are available on page 15 of this guide.

You can contact Insight on 01 674 6496 or insight@fightingblindness.ie.

How to Support Our Work

Fighting Blindness is 90% funded by you, the public, through donations and fundraising. With your help, we have invested over €15 million into 70 projects in Ireland, and we have developed a national support service through the Insight Counselling Service. It is only through your generosity and support that we are able to make a real difference.

If you would like to support the work of Fighting Blindness, please contact us to discuss your options. There are many ways in which you can support us, from a once off donation, to holding a fundraising event, running in a sponsored marathon, participating in regular giving, or by leaving a legacy in your Will.

Thank you for your continued support, hard work and dedication to making our vision a reality.

Further Information

Useful Links
Irish and International Patient Organisations
Glossary

Useful Links

Irish patient organisations supporting people with sight loss:

Fighting Blindness
W: www.FightingBlindness.ie **E:** info@fightingblindness.ie **T:** 01 6789 004

Fighting Blindness Insight Counselling Service
W: www.FightingBlindness.ie/support **E:** insight@fightingblindness.ie **T:** 01 674 6496

NCBI - The National Sight Loss Agency
The NCBI is a not for profit charity, which offers support and services to people of all ages who are experiencing difficulties with their eyesight.
W: www.ncbi.ie **E:** info@ncbi.ie **T:** 01 830 7033

Irish Guide Dogs
Irish Guide Dogs for the Blind is Ireland's national charity dedicated to helping persons who are blind or vision impaired and families of children with autism to achieve improved mobility and independence.
W: www.guidedogs.ie **E:** info@guidedogs.ie **T:** 1850 506 300 / 021 487 8200

ChildVision
ChildVision provides educational opportunities for Ireland's blind and partially sighted children and young adults.
W: www.stjosephsvi.ie **E:** info@childvision.ie **T:** 01 837 3635

Féach
Féach is a support group for parents of blind and visually impaired children.
W: www.feach.ie **E:** feachmail@gmail.com

MIST (Macular Impairment Support and Togetherness)
MIST provides support, advocacy and social / recreational activities to people with macular degeneration.
T: 01 269 1921

Irish Patient Organisations

Diabetes Ireland
Diabetes Ireland provides support and education to all people affected by diabetes. It also raises public awareness of diabetes and its symptoms and funds research into finding a cure for diabetes.
W: www.diabetes.ie **E:** info@diabetes.ie **T:** 01 842 8118 / 1850 909 909

Genetic and Rare Disorders Organisation (GRDO)
The Genetic and Rare Disorders Organisation (GRDO) is a non-governmental organisation which acts as a national alliance for voluntary groups, representing the views and concerns of people affected by, or at risk of developing, genetic or other rare disorders.
W: www.grdo.ie **E:** info@grdo.ie **T:** 086 022 9262

The Anne Sullivan Foundation for Deafblind People
The Anne Sullivan Foundation is a national organisation that was established to help low functioning deafblind children throughout Ireland.
W: www.annesullivan.ie **E:** info@annesullivan.ie **T:** 01 289 8339

Deafblind Ireland
Deafblind Ireland is an organisation set up by deafblind people, their families and professionals working in this specialist field. It seeks to raise awareness of the uniquely disabling consequences of the combined loss of sight and hearing and to provide a source of support for people who are deafblind and their families and information and guidance to professionals.
W: www.deafblindireland.ie **E:** info@deafblindireland.ie

Irish Deaf Society
The Irish Deaf Society is the largest deaf-led organisation in Ireland working with both the deaf and hard of hearing community. Their work focuses on issues such as achieving equality and access for deaf people.
W: www.irishdeafsociety.ie **E:** info@irishdeafsociety.ie **T:** 01 860 1878

Irish Resources

Irish College of Ophthalmologists (ICO)

The Irish College of Ophthalmologists (ICO) is the recognised training and professional body for medical and surgical eye doctors in Ireland. You can find your local ophthalmologist from the list on their website.
W: www.eyedoctors.ie **E:** info@eyedoctors.ie **T:** 01 402 2777

Association of Optometrists in Ireland

The Association of Optometrists Ireland is the professional representative body for the vast majority of practising optometrists in the country.
W: www.optometrists.ie **E:** info@aoi.ie **T:** 01 453 8850

Irish Platform for Patients' Organisations, Science and Industry (IPPOSI)

IPPOSI is a unique partnership of patient groups/charities, science and industry on the island of Ireland. As a patient led partnership, the platform provides a structured way of facilitating interaction between the three key membership groups (patients' organisations, scientists and industry – and where possible with state agencies) on policy, legislation and regulation around the development of new medicines, products, devices and diagnostics for unmet medical needs in Ireland.
W: www.ipposi.ie **E:** info@ipposi.ie **T:** 01 479 0552

Medical Research Charities Group (MRCG)

The MRCG is an umbrella group of medical research and patient support charities. It represents the joint interests of charities specialising in restoring health through medical research, diagnosis and treatment and, where possible, the prevention of disease. The core belief of the group is that today's health research is tomorrow's healthcare.
W: www.mrcg.ie **E:** info@mrcg.ie **T:** 01 479 3234 / 085 142 6738

Diabetic Retina Screen

The National Diabetic Retinal Screening Programme is a new, government-funded screening programme that offers free, regular diabetic retinopathy screening to people with diabetes aged 12 years and older.
W: www.diabeticretinascreen.ie **E:** info@diabeticretinascreen.ie **T:** 1800 45 45 55

Vision Sports Ireland

Vision Sports Ireland is a not for profit organisation that caters for visually impaired people of Ireland by providing sporting and recreational activities for its members throughout the country.
W: www.visionsports.ie **E:** office@visionsports.ie **T:** 01 647 2914 / 085 850 0193

International Patient Organisations

RP Fighting Blindness
RP Fighting Blindness is a medical research charity that provides support and information to people in the UK affected by retinitis pigmentosa (RP) and related conditions.
W: www.rpfightingblindness.org.uk

Usher Syndrome Coalition
The Usher Syndrome Coalition's mission is to raise awareness and accelerate research for the most common cause of combined deafness and blindness. The Coalition also provides information and support to individuals and families affected by Usher syndrome.
W: www.usher-syndrome.org

Sense
Sense is a national UK charity that supports and campaigns for children and adults who are deafblind.
W: www.sense.org.uk

Choroideremia Research Foundation
The Choroideremia Research Foundation Inc. is an international, non-profit organisation dedicated to raising funds to find a treatment or cure for choroideremia, a rare inherited retinal degenerative disease that causes blindness.
W: www.choroideremia.org

LHON Society
This LHON Society is a patient-led support group for a rare condition called Leber Hereditary Optic Neuropathy (LHON). The group is comprised of LHON patients, family members and medical professionals.
W: www.lhonsociety.org

Macular Society
The Macular Society is the national UK charity for anyone affected by central vision loss.
W: www.macularsociety.org

Retina International
Retina International is a voluntary charitable umbrella association of 33 national societies, each of which is created and run by people with retinitis pigmentosa (RP), Usher syndrome, macular degeneration and allied retinal dystrophies, their families and friends.
W: www.retina-international.org

Foundation Fighting Blindness
Foundation Fighting Blindness are a US medical research charity whose mission is to drive the research that will provide preventions, treatments and cures for people affected by retinitis pigmentosa (RP), macular degeneration, Usher syndrome, and the entire spectrum of retinal degenerative diseases.
W: www.blindness.org

European Rare Disease Organisation (EURORDIS)

EURORDIS is a non-governmental patient-driven alliance of patient organisations representing 633 rare disease patient organisations in 59 countries. They are the voice of 30 million people affected by rare diseases throughout Europe.
W: www.eurordis.org

RareConnect

RareConnect.org is an online social network for patients and families. It was created by EURORDIS (European Rare Disease Organisation) and NORD (National Organisation for Rare Disorders) to provide a safe space where individuals and families affected by rare diseases can connect with each other, share vital experiences, and find helpful information and resources. Communities for specific conditions are built in partnership with patient groups who help create, moderate and maintain the forum.
W: www.rareconnect.org/en

European Patients Forum

The European Patients' Forum is an umbrella organisation that works with patients' groups in public health and health advocacy across Europe.
W: www.eu-patient.eu

Medical and Research Links

National Eye Institute (NEI)
The NEI is one of 27 institutes and centres of the US National Institutes of Health (NIH). The NEI leads the US government's research on the visual system and eye diseases. It supports basic and clinical science programs for the development of sight-saving treatments.
W: www.nei.nih.gov

Clinical Trials.gov
ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.
W: www.clinicaltrials.gov

Vision Research EU
This "Gateway to European Vision Research" is a web-based portal service for the European vision research community and major stakeholders.
W: www.vision-research.eu

RetNet Retinal Information Network
RetNet provides tables of genes and loci causing inherited retinal diseases, such as retinitis pigmentosa, macular degeneration and Usher syndrome, and related information.
W: www.sph.uth.edu/retnet

Glossary of Terms

Amblyopia
Also known as ‘lazy eye’. Decreased vision in one or both eyes without detectable anatomic damage to the retina or visual pathways. Usually not correctable by eyeglasses or contact lenses.

Amsler Grid
The Amsler Grid is a simple screening tool used for monitoring early signs of wet AMD (age-related macular degeneration).

Angiogenesis
This is the growth of new blood vessels. When this process takes place in places where it should not, it can cause disease, such as happens in the wet form of age-related macular degeneration (AMD).

Antioxidant
This is a nutritional supplement (like vitamins C or E), drug, or naturally occurring product that protects cells from damage induced by light, stress or metabolic processes (called oxidation). Antioxidants are also prevalent in foods, such as vegetables or fruit.

Apoptosis
A controlled process for cell death, triggered by a signal or biochemical reaction, in response to an accumulation of cellular damage.

Astigmatism
Astigmatism is when the cornea (the clear cover over the iris and pupil) is more half-rugby ball shaped than the spherical, half football shape it is meant to be. The effect on the vision is to stretch out the image viewed in the area that the bulge occurs. Sometimes the brain can compensate for astigmatism although it may be too strong for this to happen without the aid of glasses.

Autosomal Dominant Disease
Disease caused when an individual inherits a disease-causing mutation in one copy of a gene pair.

Autosomal Recessive Disease
Disease caused when an individual inherits a mutation that may not cause disease unless both copies of a gene pair are mutated.

Autosome
Any chromosome within the 22 pairs of non-sex (not X or Y) chromosomes inherited by every individual from their biological parents.

Bionic Eye
A light-detecting computer chip designed to mimic basic photoreceptor cell light-detecting function that is implanted into the retina. (Also called Retinal Chip)

Cataract
Clouding of the lens is known as cataract. It can be present from birth (congenital) or can develop later in life. They are usually progressive, so require regular monitoring.

Cell
The smallest building block of a living being that is capable of functioning on its own.

Cell Based Therapy
Using cell transplants or stem cells to treat a retinal degenerative disease.

Central Nervous System
The “central command system” of the body which includes the brain, spine and retina.

Choroid
A sheet of blood vessels behind the retina that brings oxygen and nutrients and removes waste.

Chromosome
A “package” of DNA that holds the genetic code to life. In humans, each non-sex cell has 23 pairs of chromosomes.

Chronic Illness
An illness or disease that lasts a long time.

Colour Blindness
Colour blindness is the inability to identify colours in a normal way. Colour blindness is a colour vision deficiency that makes it difficult to impossible to perceive differences between some colours. Although colour blindness is usually an inherited condition, it may also occur because of eye, nerve, or brain damage, or due to exposure to certain chemicals. Colour blindness is typically identified as either total or partial, with total colour blindness being quite rare (see Achromatopsia on page --).

Cone Cell
A type of photoreceptor that detects light and is responsible for providing fine detail, daylight and colour vision.

Cornea
The clear dome or “window” that covers the front of the eye. It provides a large part of the focusing ability of the eye.

Corneal Opacity
Corneal opacities mean that the cornea, which is normally clear, has become opaque for one of a number of reasons such as dystrophy (degeneration) or scarring or cloudiness caused by dehydration or over-hydration.

Degenerative
A gradual loss of function, as in degenerative retinal diseases - a gradual loss of sight as the retina stops working.

DNA (deoxyribonucleic acid)

The chemical “blueprint” for life. Genes are made of DNA and gene mutations can cause diseases.

Dry Eye

Dry eye, known medically as keratoconjunctivitis sicca or keratitis sicca, is a condition where there is a problem with the production of tears. Usually eyes feel irritated, dry and uncomfortable. Eyes may be red and there may be a burning sensation, or it may feel as if there is something in the eye. Sometimes there may be periods of blurred vision but these normally go away after a short while or on blinking. There are three main ways to help with dry eye; preserving the existing tear flow by reducing the temperature in rooms or blinking more, using artificial tears such as drops, gels or ointments, and reducing the draining away of the tears by a process called punctal occlusion which blocks the drainage holes in the lower eyelids.

Drusen

Yellow-white retinal deposits thought to include proteins, pigments and fats. Dry AMD or juvenile macular degeneration may occur when drusen become too large or numerous and collect around the macula.

Electroretinogram (ERG)

This is a test carried out by your eye doctor. It measures the electrical response of the light sensitive cells in the eye, the rods and cones, it also measures retinal function.

Flashes and Floaters

Flashes and floaters are a very common occurrence for many people. Floaters are little specks or threads that sometimes drift across the line of vision and flashes are little sparks of light that sometimes flicker across the visual field. Both are usually harmless but in some cases they can be a warning sign of trouble in the eye. If your flashes and floaters become more plentiful, you should consult your doctor for an eye exam.

Fluorescein Angiogram

This is a test carried out by your eye doctor. A dye, called fluorescein, is injected into the bloodstream and highlights the blood vessels in the back of the eye so they can be photographed.

Fovea

A small pit at the centre of the macula with a high concentration of cone cells.

Free Radical

A highly reactive chemical or nutritional breakdown product that can cause damage to a cell or tissue.

Fundus

The interior surface of the eye that includes the retina, fovea and macula.

Fundus photographs

These are carried out by your eye doctor to look for any changes or abnormalities in the back of the eye.

Gene

A unit of inheritance, encoded by DNA. These stores of information tell our cells what to do and pass down family traits including hair and eye colour, as well as certain diseases. If there is a mutation in a gene, this may cause a disease.

Gene Mapping

Identifying a region of a chromosome that is responsible for causing a disease (or causing some known function), but not yet identifying the exact gene.

Gene Therapy

A therapeutic process that replaces or turns off the faulty or mutated disease causing gene and restores some level of normal protein function.

Genetic Testing (also known as Genotyping)

Generally, this is defined as determining the genetic make-up of an individual. Specifically, it is looking for the gene(s) that cause an individual's retinal degenerative disease.

Genetics

The study of inheritance. Specifically, it is the determination of genes linked with causing retinal degenerative disease.

Geographic Atrophy

This may be considered the end stage of dry age-related macular degeneration (AMD), causing severe vision loss. Over time, sometimes over many years, the atrophy of the RPE cells (due to drusen deposits in the retina) gets more prevalent with all of the macula being affected.

Glaucoma

Glaucoma is the name for a group of eye conditions which cause damage to the optic nerve, typically caused by a clinically characterised pressure build-up in regards to the fluid of the eye (intraocular pressure-associated optic neuropathy). Early detection and treatment can limit vision loss due to glaucoma.

Hyperopia

Also known as hypermetropia, hyperopia is long sightedness. When a person is long sighted, this means that they can see objects that are further away more easily than those that are nearer to them. Most people will have glasses that they need to wear for reading, watching TV, table top activities etc. This is because the eyes struggle to focus at all distances and this, if uncorrected, can lead to eyestrain.

Intra Ocular Injections

This refers to injections directly into the eye

Intra Ocular Pressure

Increased pressure within the eye. e.g. Glaucoma.

Iris

The coloured “ring” that regulates the amount of light that is admitted into the eye.

Keratoconus

This is a degenerative condition where the cornea thins and is pushed outwards, usually in the centre, by the internal pressure of the eye. Usually this is hereditary, occurs in both eyes and appears in the teens. It is associated with conditions such as Downs Syndrome. If untreated, it can result in a rupture, but sometimes it may stop in an earlier stage of its development or simply not progress that far. It is a condition which requires regular monitoring. In mild cases, spectacles will offer correction of the refractive problems. Contact lenses may be required for more advanced cases.

Lens

The transparent part of the eye that focuses light onto the retina, so that we can see.

Lutein and Zeaxanthin

Nutrient pigments chemically related to beta-carotene that are abundant in green leafy vegetables and yellow and orange- coloured fruit and vegetables. These are the only two known food pigments that collect in the macula, where they are thought to protect it from light damage (blue light).

Macula

The centre of the retina that has a concentration of cone photoreceptor cells and is responsible for fine detail, day and colour vision.

Macular Hole

Macular hole is a problem that affects the very central portion of the retina. It happens for a variety of reasons such as eye injuries, certain diseases, and inflammation inside the eye. However, the most common cause is related to the normal aging process. Macular holes often begin gradually and affect central vision depending on the severity and extent of the problem. Partial holes only affect part of the macular layers, causing wavy, distorted, blurred vision. Patients with full-thickness macular holes experience a complete loss of central vision. Some macular holes seal spontaneously and require no treatment. In many cases, surgery is necessary to close the hole and restore useful vision.

Mutation

A change or “spelling mistake” in the DNA of a gene that can cause a disease (but not always).

Myopia

Myopia is short sightedness. This means that the eye has difficulty when focussing on more distant objects; so glasses should be worn when prescribed.

Neuroprotective Therapy

Delivering a protein or drug to the eye that prevents the photoreceptors and/or RPE cells from dying.

Nucleus

The specialised compartment within a cell that houses DNA.

Nystagmus

Nystagmus is a constant, rapid and involuntary oscillation of the eyes – one of the symptoms that can be experienced by patients who have a retinal degenerative disease, like Leber congenital amaurosis. This is a condition where the eye moves almost constantly. It can either be vision related or due to muscular imbalance. If vision related, it often indicates deterioration in the central field of vision, such as macular degeneration or loss of central vision. It occurs as the eye is relying largely on rod cells in the peripheral retina which require movement to focus on an object or else it will fade out. If the object is not moving then the eye will move as it attempts to keep the object in focus.

Ophthalmologist

A medical doctor specialising in the eye that can carry out specialised treatments or surgery.

Optic Nerve

The bundle of nerve cells, or “cable” that transmits signals from the retina to the visual processing centre of the brain.

Optician

Someone who makes or sells lenses (glasses or contacts) in accordance to an optometrist’s prescription.

Optometrist

A licensed professional who examines your eyes for defects in vision or eye conditions in order to prescribe corrective lenses or appropriate treatment.

Oxidative Stress / Oxidation

Oxidation is the interaction between oxygen molecules and all the different substances they may contact. Oxidative Stress can occur when there is an imbalance, and a biological system cannot readily detoxify or easily repair the resulting damage, thereby promoting development of a retinal degenerative disease.

Papilledema

Usually results from a head injury. Optic disc appears raised above the level of the retina.

Pathological (Degenerative) Myopia

Pathological myopia is a rare type of shortsightedness where the eyeball continues to grow, becoming longer than it should be. Pathological myopia is quite different from the simple refractive myopia or nearsightedness that affects so many people

around the world. In people under age 50, pathological myopia is often associated with the growth of leaky blood vessels that grow in the back of the eye, a condition your doctor may call choroidal neovascularisation. The development of choroidal neovascularisation is associated with serious impairment of vision and, in some cases, profound vision loss.

Phenotype
Physical symptoms of a retinal degenerative disease that can be clinically defined. Each phenotype is normally associated with a particular genotype (see Genetic Testing).

Photodynamic Therapy
A therapy for the wet form of AMD that involves using a drug and a “cold” laser to destroy new, unwanted blood vessels.

Photoreceptor Cells
The light-sensitive cells (rods and cones) in the retina.

Presbyopia
This is a refractive condition in which the accommodative ability of the eye is insufficient for near vision work due to ageing.

Proof of Principle
The first measurable evidence that an experimental theory or therapy works.

Retina
The thin layer of light-detecting cells at the back of the eye.

Retinal Chip
A light-detecting computer chip designed to mimic basic photoreceptor cell light-detecting function that is implanted into the retina. (Also called Bionic Eye).

Retinal Pigment Epithelium
A very thin layer found directly beneath the photoreceptor cells. RPE cells bring nutrients and oxygen to the photoreceptor cells, and supplies, recycles and detoxifies products involved with the phototransduction process.

Retinal Prosthetic
An implantable device that electrically stimulates the retina with information that it receives from a secondary light detection device (i.e. camera, glasses).

Retinal Tear / Detachment
Retinal detachment is a condition where the retina separates from the underlying choroid layer of the eye. Retinal detachments have many causes, including aging, surgery, trauma, inflammation, high myopia and diseases such as diabetic retinopathy, retinopathy of prematurity and scleritis. Symptoms include light flashes, floaters, shadow coming down over vision, blurred vision and vision loss. A retinal tear often occurs before a detachment. When the fluid migrates beneath the retinal tear, it can

lift the retina off of the back of the eye leading to detachment. Surgical outcomes have now vastly improved in recent years and anatomic re-attachment of the retina most often leads to recovery of at least some visual function. Visual outcomes are best when the detachment is discovered and treated without delay.

Retinopathy of Prematurity

Retinopathy of Prematurity (ROP), also known as retrolental fibroplasia, is a potentially blinding condition affecting the retina of newborns. ROP mainly affects the retinal blood vessels. When the development of the retinal blood vessels is incomplete, the retina is not receiving enough oxygen so tries to grow new vessels. These new vessels are fragile and cause scarring. The factors that put infants at greatest risk of developing ROP are low birth weight (less than 3.5 pounds) and premature delivery (26-28 weeks). The overwhelming majority of these babies will have mild ROP and will not require treatment. Although the incidence of ROP is on the rise due to increased survival of very premature babies, medical advances mean fewer babies require treatment. If treatment is required, laser therapy is used to stop the growth of these blood vessels. Other therapies including Anti-VEGF injections are currently being explored for their effectiveness in ROP.

Rhodopsin

A light detecting component (a visual pigment) of rod photoreceptor cells composed of a protein called opsin that is chemically linked to a processed fragment of vitamin A.

RNA

A family of gene products whose most common member, messenger RNA (mRNA), is used as a template for making protein.

Rod Cell

A photoreceptor cell responsible for black and white, night and peripheral (side) vision.

Sclera

The white, tough, outer, protective shell of the eye.

Stem Cell

A self-renewing, unspecialised cell that is capable of becoming any one of a number of more specialised cells.

Strabismus

A strabismus is basically a squint. The main effects of a strabismus are that usually the person will have one eye that is stronger than the other. This is because the brain has to give priority to one eye over the other with the result that the weaker one does not ‘learn’ to see as well as the stronger one. In practical terms, a person should be guided from their weaker side to allow them to make full use of their stronger eye, but in contrast, should be approached from or have objects presented to their stronger side.

Sub Retinal Injection

This refers to injections that are given directly into the sub retinal space.

Vector

The “vehicle” or carrier for delivering genes or genetic information into the cells, particularly useful for gene therapy.

VEGF

A class of proteins that cause new blood vessel growth (angiogenesis) and maintains the natural “leakiness” inherent in vessels. These are normal body functions, but if they happen where they shouldn’t (such as in the retina), they can cause disease, such as AMD.

Visual Acuity

A measure of the ability to distinguish fine visual details.

Visual Cycle

The process of detecting light and converting it to an electrical signal that is then relayed to the brain via the optic nerve.

Visual Field

The entire area that the eye can see from side to side without physically moving the eyes or head (includes peripheral vision).

Vitreous

The clear, jelly-like substance found in the middle of the eye that helps to regulate eye pressure and shape.

X Chromosome

The inherited package (or chromosome) of DNA that contains genes that help to determine the sex of an individual. Two X chromosomes are inherited by females, while one X chromosome and one Y chromosome are inherited by males. Mutation of a gene found on the X chromosomes can cause X-linked diseases.

Y Chromosome

The chromosome (DNA package) passed down from biological father to son that contains genes that determine male gender.

Zeaxanthin and Lutein

Nutrient pigments chemically related to beta-carotene that are abundant in green leafy vegetables and yellow and orange- coloured fruit and vegetables. These are the only two known food pigments that collect in the macula, where they are thought to protect it from light damage (blue light).

Fighting Blindness
Fighting Blindness is an Irish charity enabling world-leading research into treatments and cures for blindness. It also provides a professional counselling service for people and families affected by sight loss, and is extremely active in the area of advocacy and patient empowerment.

Fighting Blindness is involved with rare, genetic, age-related and degenerative conditions that affect an estimated 224,000 adults and children in Ireland and 285 million worldwide. Please contact 01 6789 004 or info@fightingblindness.ie for more information or visit www.FightingBlindness.ie.

Bayer Healthcare
Bayer: Science For A Better Life

Bayer in Ireland is part of the global organisation Bayer AG, based in Leverkusen, Germany, with 114,928 employees worldwide and over 100 employees in Ireland. For over forty five years, we have developed quality medicines for diagnosing, combating and preventing disease in Irish patients. We are involved in researching new pathways, new molecules, and new technologies in areas with a high level of unmet medical need, such as cancer therapy, cardiovascular and blood disorders, as well as gynaecology and ophthalmology.

For over 30 years Fighting Blindness has been working towards finding a cure for blindness. The future has never been brighter for patients. By working together, we believe we can make this vision a reality.

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